

In this article published in 1953, Dr. Fred Klenner reviews some of his experiences using injections of vitamin C to treat a variety of diseases including viral pneumonia and encephalitis following measles and polio. He describes how he discovered that injectable vitamin C can be used as an antibiotic to treat many diseases.—*R.D.M.*

The Use of Vitamin C as an Antibiotic

Fred R. Klenner, M.D., Reidsville, N.C.

Journal of Applied Nutrition, 1953, Vol. 6, pp. 274–278

VITAMIN C—the foundation of the oxidation-redux system now through greater dosage reveals its outstanding qualities as a non-toxic antibiotic.

On the 11th of December 1621 Edward Winslow,¹ one of the Pilgrim Father's, writing to a friend in England who was about to make the trip to the new world gave this advice:—"Bring juice of lemons; and take it fasting. It is of good use." Three hundred and eleven years later, 1932, and also in December, Waugh and King² found that this 'important' lemon juice contained a six carbon chain acid which is now known as vitamin C. Ascorbic acid is related to the hexuronic acids which in turn are derivatives of the simple sugars (Youmans 1941³). The value of this vitamin as an essential factor for life is universally known and accepted. The importance of vitamin C as an antibiotic and as the pre-cursor of antibody formation lack scientific appreciation because of its simplicity, and because of the reluctance on the part of the medical profession to employ it in massive doses administered like other antibiotics—around the clock. Allergy has become a major problem since the advent of the mold-derived drugs. Hippocrates did declare that the highest duty of medicine to be to get the patient well. He further declared that, of several remedies physicians should choose the least sensational.

To understand the antagonistic properties of vitamin C against the virus bodies and also against the chemical ferments of micro-organisms—the toxins and exotoxins, one must go beyond its present academic status as a factor essential for life. A striking phenomena of vitamin C is the similarity of response either to correct pathology due to a deficiency of this compound, or to correct the pathology caused by the action of the virus bodies and other similar toxins and ferments. Within a few hours after adequate vitamin C therapy is instituted **by needle** one will find in the deficiency syndrome that fibroblasts are beginning to form normal connective tissue and that capillary buds are invading blood clots and other types of hemorrhagic areas (Youmans 1941³). Likewise when employed as an antibiotic definite clinical response is made evident by a climb-

Paper presented at AAN Convention, May 1953, Pasadena, California.

ing white blood count, drop in fever and general all around improvement of the patient within the same time schedule.

For many years it has been the accepted thought of the medical world that the forcing of citrus fruit juice in infections of the chest and upper respiratory areas, particularly by virus bodies, was valuable in that it produced alkalinity of the body fluids by way of its residue, the alkaline ash. This premise held that in this alkaline state greater phagocytic possibilities was allowed the leukocytes in destroying bacteria. This theory, although correct for the usual bacterial flora, was never too plausible for virus diseases since a leukopenia rather than a leukocytosis exist in these conditions. In the 1948 poliomyelitis epidemic in North Carolina we observed a greater response to vitamin C given by mouth when rutin was added.² The alkaline ash here serving as a barrier to the loss of vitamin C by way of the kidneys. Vitamin C is excreted by glomerular filtration and is resorbed by the tubules. There is a maximum rate at which the tubules can resorb, so it is real economy to keep the urine alkaline. Hawley and her associates⁴ (1936) reported that the quantity of vitamin C excreted may be varied by merely changing the acid-base balance of the food intake.

Our interest with vitamin C against the virus organism began ten years ago in a modest rural home. Here a patient who was receiving symptomatic treatment for virus pneumonia had suddenly developed cynosis. He refused hospitalization for supportive oxygen therapy. X-Ray had not been considered because of its dubious value and because the nearest department equipped to give such treatment was 69 miles distant. Two grams of vitamin C was given intramuscularly with the hope that the anaerobic condition existing in the tissues would be relieved by the catalytic action of vitamin C acting as a gas transport aiding cellular respiration. This was an old idea, the important factor being that it worked. Within 30 minutes after giving the drug (which was carried in my medical bag for the treatment of diarrhea in children) the characteristic breathing and slate-like color had cleared. Returning six hours later, at eight in the evening, the patient was found sitting over the edge of his bed enjoying a late dinner. Strangely enough his fever was three degrees less than it was at 2 P.M. that same afternoon. This sudden change in the condition of the patient led us to suspect that vitamin C was playing a role of far greater significance than that of a simple respiratory catalyst. A second injection of one gram of vitamin C was administered, by the same route, on this visit and then subsequently at six hour intervals for the next three days. This patient was clinically well after 36 hours of chemotherapy. From this casual observation we have been able to assemble sufficient clinical evidence to prove unequivocally that vitamin C is the antibiotic of choice in the handling of all types of virus diseases. Furthermore it is a major adjuvant in the treatment of all other infectious diseases.

This experimental 'strike' on vitamin C as an antibiotic opened a new avenue of approach to the problem of dealing with the virus bodies. With a great deal of enthusiasm we decided to try its effectiveness with all of the childhood diseases. Measles was singled out more so than the others because of the knowledge that it was a small virus like the one causing poliomyelitis. It was reasonable to assume that if measles could be controlled then Poliomyelitis, too, would have a drug that could prevent as well as cure the disease. The use of vitamin C in measles proved to be a medical curiosity. For the first time a virus infection could be handled as if it were a dog on a leash. In

the Spring of 1948 measles was running in epidemic proportions in this section of the country. Our first act, then, was to have our own little daughters play with children known to be in the 'contagious phase.' When the syndrome of fever, redness of the eyes and throat, catarrh, spasmodic bronchial cough and Koplik spots had developed and the children were obviously sick, vitamin C was started. In this experiment it was found that 1000 mg every four hours, by mouth, would modify the attack. Smaller doses allowed the disease to progress. When 1000 mg was given every two hours all evidence of the infection cleared in 48 hours. If the drug was then discontinued for a similar period (48 hours) the above syndrome returned. We observed this off and on picture for thirty days at which time the drug (vitamin C) was given 1000 mg every 2 hours around the clock for four days. This time the picture cleared and did not return. These little girls did not develop the measles rash during the above experiment and although exposed many times since still maintain this 'immunity.' Later cases were given the vitamin by needle. The results proved to be even more dramatic. Given by injection the same complete control of the measles syndrome was in evidence at 24 and 36 hour periods, depending entirely on the amount employed and the frequency of the administration. Aborting of these cases before the development of the rash apparently gives no interference to the development of immunity. Recent progress on the rapidity of growth (or development) of the virus bodies by means of the electronic microscope makes intelligent the failure experienced by earlier workers when employing vitamin C on the virus organism (or bodies). Unless the virus is completely destroyed, as demonstrated in the experiments with the virus causing measles, the infection will again manifest itself after a short incubation period. Small, single daily doses do not even modify the course of the infection. From a review of the literature one can safely state that in all instances of experimental work with ascorbic acid on the virus organism, in experimental animals, the amount of virus used was far beyond the range of the administered dose of this vitamin. It is timely to note here that all of our re-search with vitamin C on the virus was done, using MAN as the experimental animal. This makes an important difference. For example the signs of acute and chronic vitamin C deficiencies in the monkey are **DISTINCTLY DIFFERENT** than in man. This may partially explain the difference observed in experimentally produced and spontaneous scurvy in man. (Shaw et al. 1945⁵). This would seem to disprove the opinion of Thomas M. Rivers⁶ (1941) when he writes, "On the other hand, a few investigators (Heaslip, McCormick, Stern, Tebbutt & Helms) have recorded what might be considered very poor evidence, obtained by observations on human beings, that vitamin C deficiencies play a role in susceptibility to poliomyelitis." The accuracy of Rivers evaluation of these works relating to these observations seems questionable when he states (1941)⁶ that Sabin (1939)⁷ definitely demonstrated that Jungeblut's (1937⁸⁻⁹) claim that Vitamin C deficiency increases the susceptibility of the experimental animals to infantile paralysis is not valid. Jungeblut (1937)⁹ stated that the parenteral administration of natural vitamin C during the incubation period of poliomyelitis in monkeys is always followed by a distinct change in the severity of the disease; that after the fifth day of the disease **LARGER** doses are required. He realized, at that early date, that for a fast progressing infection such as results from the R.M.V. strain, very large doses must be

given; for the Aycock virus with its slower infection potential small amounts of vitamin C would suffice. During the 1948 Polio epidemic in North Carolina it was our humble privilege to observe and report (1949)¹⁰ that a 'period of septicemia did exist in the first few days of poliomyelitis.' It was our impression at that time that the virus multiplied on a living tissue, the blood, and that the time to destroy the virus was during this 'incubation period' which varies more with the virus strain, its virulence and power of multiplication than with the size of the initial dose. Bodian and Horstmann (1952)¹¹ confirmed our observation of the existence of a viremia phase in poliomyelitis, demonstrating that the virus was freely present in the blood of chimpanzees during the preparalytic period of the disease.

One of the most unfortunate mistakes in all of the research on poliomyelitis was Sabin's UN-SCIENTIFIC attempt to confirm Jungeblut's work with vitamin C against the Polio virus in monkeys. Jungeblut in infecting his Rhesus monkeys used the mild 'droplet method' and then administered vitamin C by needle in varying amounts up to 400 mgm/day. Even this method did not give him absolute control over the degree of infection that would result. However, his antibiotic (vitamin C) remained relatively constant. With almost infinitesimal amounts, as we at present recognize, he was able to demonstrate in one series that the non-paralytic survivors was six times as great as in the controls. On the other hand, Sabin, in infecting his monkeys did not follow the procedure given by Jungeblut who's experiments he was attempting to repeat, but instead employed a more forceful method of inoculation which obviously resulted in sickness of maximum severity. Sabin further refused to follow Jungeblut's suggestion as to the dose of vitamin C to be used. By Sabin's actual report the amount given was rarely more than 35 per cent of that used by his associate. Sabin makes this significant statement (1939)⁷, "One monkey was given 400 mgm of vitamin C for one day at the suggestion of Jungeblut who felt that large doses was necessary to effect a change in the course of the disease." Yet on the basis of Sabin's work the negative value of vitamin C in the treatment of virus diseases has been for years accepted as final.

For some unexplained reason vitamin C has been 'tied up' with scurvy to the exclusion of its many other functions. Those who would have us believe that this vitamin serves no other purposes argue that there is no evidence to substantiate the claim that malnutrition plays a definite role in susceptibility to the virus infections. We are invited to read what Aycock wrote in 1937 concerning "the tendency of poliomyelitis to occur in children who are large, healthy and well nourished." What is important we are not told. Of course, Polio, like any other childhood disease, is not dependent on specific personalities or certain constitutional types. The real reason for it developing and doing so in varying degrees is due to some other cause. Surely measles doesn't limit its attack to the frail, unstable child or adult.

The exact incident of vitamin C deficiency is unknown. No accurate way of determining whether a deficiency of vitamin C exists in the body tissues has been developed (Thewlis Clinic¹² 1953). There is increasing evidence to indicate that a relatively large number of persons have hypovitaminosis C (Vitamin C deficiencies) and that these include individuals whose diets are generally considered satisfactory (Youmans 1941³). The National Research Council recommends 75 mgm./day as the minimum requirement

(1945). This is only a measure of the amount necessary to prevent gross disease and is not a measure of the amount needed to maintain good health. Kline and Eheart¹³ (1944) reported wide variations in the need for vitamin C in normal individuals. Jolliffe¹⁴ (1945) suggested that the optimum requirements may actually be ten or more times the recommended minimum daily requirements. Under certain conditions 1000 mg. to 3000 mg. per day were found by Kyhos et al.¹⁵ (1945) to be necessary to keep the body saturated. There is a wide individual variation in the renal threshold for vitamin C. Many patients receive as much as 1500 mg. of vitamin C per day without significant urinary loss (Shaw 1945)⁵. All of us have witnessed 'nose bleed' in certain children sick with measles who prior to taking the disease were apparently healthy. Epitaxis (nose bleed) is one of the signs of scurvy. Is this true scurvy? Crandon¹⁶ (1940) states that scurvy develops slowly in man. He found the vitamin C level of the blood plasma to be zero for 90 days before there was frank clinical evidence and that this was as long as 132 days before the first signs appeared. He reported that 1000 mg. of vitamin C was given daily for two weeks to clear skin petechiae. I have, many times, stopped nose bleed in children, sick with measles, with one single dose of 2 gms. Vit. C.

Dolldorf¹⁷ (1945) reported that many conditions may be present in the body that call for a greater supply of vitamin C. He lists fever, infection, physical stress, gastrointestinal disorders, diarrhea, anorexia, and vomiting along with many others. It is of more than academic interest to observe that all of the above listed conditions are usually found in severe cases of poliomyelitis. One wonders whether or not these are manifestations of vitamin C deficiencies or true findings of the Polio syndrome. Certainly we do see several, if not all, of these symptoms associated with other childhood diseases. We have also found that like epistaxis all of the above mentioned conditions can be relieved with one or two injections of vitamin C, the amount ranging from one to four grams depending on the age of the patient. These manifestations represent acute vitamin C loss and is Nature's way to ask for help. There exists a possible avenue of escape from this clinical pattern and that is to watch for the sign post that reveal pre-existing chronic vitamin C deficiencies. Shaw⁵ (1945) states that food deposits on our teeth and dental tartar represents this condition. People who find that they are counted in this group should supplement their diet with at least two grams of vitamin C each day, or drink not less than three, 200 c.c. size, glasses of orange juice for the same period.

To support our findings that massive doses of vitamin C is a potent antibiotic several case histories follow:—

Case I—Measles in a ten-months-old baby. The infant had a fever of 105(R) F., redness of eyes and throat, catarrh, spasmodic bronchial cough and Koplik spots. 1000 mg. of vitamin C was given intramuscularly every four hours. After 12 hours the fever was 97.6 (R) F., the conjunctivitis and red throat had cleared, there was no cough. The sudden drop in the fever curve was thought to be explainable on one of three grounds: 1) Common night drop. 2) Due to the antibiotic action of vitamin C. 3) Even if the vitamin C injections had been continued, a moderate rise might have occurred in the late afternoon of the second day, granting a highly virulent organism and a poorly resisting host. To determine which of these deductions was valid, vitamin C was discontinued for a period of eight

hours. At this point the rectal temperature reading was 103.4 F. Vitamin C therapy was resumed and instead of the expected 8 P.M. climb, the fever was down to 99.2 (R). The 1000 mg. injections were continued as before, the baby made an uneventful recovery and was discharged 60 hours following hospital admission. No measles rash developed. Four years have now elapsed and there has been no measles.

Case II—A case of virus pneumonia with typical consolidation of an entire lung field. Patient colored female, age 28. Relative gave history of chills, fever, head and chest cold for past 14 days. In stupor when first seen, eye lids closed, a white foam at the mouth which she periodically tried to spit out. Fever by axilla 106.8 F. (corrected). Dehydration was much in evidence, breath sounds diminished to absent, tactile fremitus increased over the entire right side. The sulfa drugs, penicillin and streptomycin with supportive treatment had been exhausted by the referring physician. Four grams of vitamin C was given intravenously along with 1000 c.c. dextrose 5 in saline solution. Temperature dropped to 100 (Ax.) corrected within eleven hours. Four hours later, vitamin C was resumed, the dose ranging from 2 to 4 grams every two to three hours depending upon the response. After 72 hours the patient was awake, sitting up in bed and taking fluids freely by mouth. There was no fever at this time, nor for the remainder of the time in hospital. Vitamin C was continued for two weeks; the frequency was cut to every 12 hours, two grams at a dose. The rationale of this continued use of vitamin C was to assist the body to clear up the debris in the right lung field. Although the patient was clinically recovered, it required three months to clear the lung by X-ray. In this Nature was merely duplicating a stage in the metamorphosis of the frog in getting rid of its tadpole tail.

Case III—A case of encephalitis following measles and mumps. This was a lad of eight years first seen with a fever of 104 F. He was lethargic, very irritable when molested as in simple physical examination. His mother said he had gradually developed his present clinical picture over the preceding four or five days. His first symptom was anorexia which became complete 36 hours before his first visit. He next complained of a generalized headache, later he became stuporous. Although very athletic and active, he voluntarily took to his bed. He was given 2000 mg. of vitamin C intravenously and allowed to return home because there was no available hospital accommodations. His mother was asked to make an hourly memorandum of his conduct until his visit set for the following day. Seen 18 hours after the initial injection of vitamin C, the memorandum revealed a quick response to the antibiotic—after two hours he asked for food and ate a hearty supper, then played about the house as usual and then, for several hours, he appeared to have completely recovered. Six hours following the initial injection, he began to revert to the condition of his first visit. When seen the second time temperature was 101.6 F, he was sleepy but he would respond to questions. The rude irritability shown prior to the first injection of vitamin C was strikingly absent. A second injection of 2000 mg. was given intravenously and 1000 mg. of 'C' prescribed every two hours by mouth. The next day he was fever- and symptom-free. As a precautionary measure a third 2000 mg. was given with directions to continue the drug by mouth for at least 48 hours. He has experienced no residual cerebral pathology as determined by examination five years

following this episode. (Similar cases seen in the interim have shown more dramatic response when the drug was given by needle every two to four hours.)

Case IV—POLIOMYELITIS. A boy of eight years was brought to my office with a history of having had 'flu' for a period of one week. Four days before this office visit he developed photophobia, conjunctivitis, sore throat, back-of-the-eyes type headache, nausea and vomiting. The headache was of such intensity that adult doses of aspirin given by his mother had no effect. While on the examining table the boy was either rubbing his neck on the left side or holding his head between his hands, begging for something to relieve his pain. The fever was 104.4 (Ax.) F. He was tender in the lumbar region and he had a drawing sensation referred to the hamstring attachments at the left knee. Two grams (2000 mg.) of vitamin C was given intravenously while in the office. He was sent to the local hospital where he received, promptly, a second injection of 2 grams of the vitamin, after which it was given every four hours. Six hours after commencing therapy the neck pain was gone, the headache completely relieved (he did not receive pain relieving medication), he could tolerate the ceiling light, his eyes were dry and the redness was definitely clearing. Nausea and vomiting had disappeared, the fever was down to 100.6 (Ax.) F., and he was sitting up in 'a straight positioned bed' in a jovial mood while he drank a glass of lime ade. He was discharged from the hospital after receiving 26 grams of vitamin C in 48-hour period, clinically well. Vitamin C was continued by mouth, 1500 mg. every two hours taken with citrus fruit juice. This schedule was followed for one week after which time a change was made to Vitamin B₁, 25 mg. before meals and bed hour. Vitamin B₁ was given in view of McCormick's¹⁸ (1938-1939) theory that inflammatory and degenerative diseases of the nervous system is due to an avitaminosis of this particular vitamin. Vitamin B₁ in these cases should be continued for a period of at least three months as nerve tissue is slow in recovering from even mild damage.

The amount of vitamin C for optimum effect will vary greatly with the individual. The type of the disease and the degree of toxemia (or viremia) are important guides in determining the dosage. Although the usual dose of vitamin C is calculated on the basis of 65 mg. per Kg. of body weight, and given every two to four hours by needle, under certain conditions larger single injections can be used to good advantage. In using 'C' as an adjuvant in the treatment of infections caused by the more common bacteria the single 250 mgm. per Kg. of body weight injection behaves like other synergistic drug combinations. Likewise when treating an upper respiratory infection, this one single massive 'shot' will precipitate the pathology. A report from the Thewlis¹² Clinic (1953) is interesting in this respect—"Upper respiratory tract infections may severely tax the vitamin C reserve. It is usually during or following a cold that patients have epistaxis or cough up blood-streaked sputum. Local inflammation and **depletion** of vitamin C may be responsible for this hemorrhagic tendency. On numerous occasions, we have observed a dramatic alleviation of symptoms of [an] upper respiratory tract infection after an injection of 500 mgm. of ascorbic acid (vitamin C)." Vitamin C response when taken by mouth is not predictable. Wright and Lilienfeld¹⁹ (1936) reported that the ascorbutic

state could develop even though the patient was taking large doses of vitamin C by mouth. In the opinion of Musser²⁰ (1945) poor absorption and equally poor storage are cardinal factors in leading to vitamin C deficiencies. It was our privilege to observe this mechanism in one of our daughters several years ago. She had contracted chicken-pox. Vitamin C was started on this child when the macules first put in their appearance. In spite of the fact that she was given 24 grams every 24 hours there was no interruption in the progress of the disease. Itching was intense. One gram administered intravenously stopped the itch within 30 minutes and she went on to peaceful sleep for the next eight hours. Although feeling fine, a second injection was given at this time, following which there were no new macules and recovery was fast and uneventful. In the past few years we have noted that in chicken-pox when massive injections are employed there is no repeating waves of macules, and the usual seven to nine days required for crusting is reduced to less than twenty-four hours. Large doses parenterally are effective when oral administration fails (Youmans 1941)³.

It is not uncommon to find a patient sick with a virus disease that is also being subjected to the effects of the toxins of a 'secondary invader.' This problem of mixed infection is usually found in virus pneumonia and infectious mumps. The mouth, nose and naso-pharynx represent 'living space' for many micro-organisms. Therefore it is possible to have parotitis secondary to buccal surgery without virus contamination, but it is never possible to have infectious parotitis (mumps caused by the virus organism) without secondary invading pathogenic organisms. In treating virus pneumonia and 'Virus' mumps it is necessary either to give one or two injections of penicillin along with the vitamin C or comparable sulfa therapy. In the case of mumps it would seem from an academic point of view that Aureomycin would serve this purpose better since it does have antibiotic possibilities with the **large** virus organisms. The antibiotic power of vitamin C can also be augmented by other biochemical fractions. One of these is a colloidal solution of denatured proteolytic enzyme called 'PROTAMIDE.' In Herpes Simplex and Herpes Zoster this 'enzyme' proved to be of definite value, and in Herpes Zoster (Shingles) did influence the dorsal nerve root pain. Of course it is common knowledge that vitamin C, especially when injected intramuscularly, possesses these same anti-neuritic properties. Vitamin C, itself, can be called a 'cousin' of the proteolytic enzymes. This suggested that vitamin C and protamide should be used at the same time. The clinical results justified this assumption. Cures were obtained in from one to three days. Vitamin C was given as usual, but protamide was limited to one ampule per day. The same 'improved' results were obtained in influenza and definite synergistic action was seen in one case of poliomyelitis in a boy of ten years. Calcium, too, is a good adjuvant especially in treating influenza. In vivo calcium duplicates the chemical behavior of vitamin C in many respects. Whether the virus has some destructive influence over the calcium ions is a matter of debate. From our experience it would seem that the inclusion of at least one 10 c.c. vial of calcium gluconate or calcium levulinate in the treating of a virus infection is good therapeutics. Levulinate must be injected at a slower rate than Gluconate. Calcium gluconate can be injected intramuscularly, in adults, if veins are at a premium, but it must be placed deep in the gluteal muscle. Vitamin C and D.C.A. 2 mg. to 5 mg. (the latter once/day) proved to have definite value against the influenza virus in recent tests.

We reported in 1951 and 1952 that a constant laboratory finding in virus infections was a positive, qualitative Benedict's reaction. It is necessary to make a correction of that finding. This Benedict's reaction was based on the admission urine specimen of patient's admitted to our local hospital. About six months ago it came to my attention that this particular urine specimen is collected anytime from the admission of the patient to the hospital until some 18 hours thereafter. This, obviously, nullifies the laboratory report since medication given to the patient in the interim would alter the chemical findings. Vitamin C being a powerful reducing agent could account for some of the Benedict urine reports. It, therefore, makes void the contention that this laboratory test is an index when to discontinue the use of vitamin C. The deduction, however, is correct. We have ascertained during the past six months that this glycosuria ranges from a quantitative increase over a given patient's normal range to a qualitative 2 plus. The majority of severe virus infections will show a strong trace Benedict's qualitative reaction. Individual kidney threshold for sugar and/or vitamin C is probably a factor in the higher readings.

Pathologic changes due to excessive amounts of vitamin C are unknown. Plasma concentrations twenty times normal have been obtained without any ill effects (Youmans³ 1941). Occasionally there may be a sensitivity to common foods rich in vitamin C and constitutional idiosyncrasies to ascorbic acid [do] exist. These minor complications are Diarrhea, Induration (only when intramuscular injections are given too close to the surface), Endothelial irritation, Venous thrombosis (only when the concentration of the solution is 500 mg. per c.c. or greater), Syncope (only in patients over 50 years of age if the injection is made too rapid), Rash and vulvitis and puritis. This last factor was seen in ½ of 1% of children given massive therapy of the vitamin by mouth over a long period of time. Derma medicone ointment will control these symptoms. The vitamin should be discontinued by mouth, if this occurs, and given by needle. We have found that a No. 23 G needle ¾ inch long is ideal for intravenous use and a No. 22 G needle one inch long for the intramuscular routes. A needle 1½ inches long if the latter route is employed in adults.

Fortunately vitamin C is a vitamin supplied by Nature in a variety of foods. Foods rich in vitamin C are citrus fruits (lemons, limes, oranges, and grapefruit), tomatoes, pineapples, currants, raspberries, strawberries, green vegetables such as peas, beans, lettuce, asparagus, broccoli, brussel sprouts, young cabbage, cauliflower, chard, collards, kale, parsley, kohlrabi, peppers, squash, turnips, and greens of various kinds. Milk is only a fair source of vitamin C. Vegetables should be eaten raw when possible; when this is not feasible they should be cooked in as short a time as possible and in a small amount of water, which should be boiling before foods are added. Raw cabbage is an excellent source, but if allowed to stand will rapidly lose its vitamin content. Storage, processing, cooking and the variability of different samples of fruits are factors of importance. Storage and handling have relatively little effect on such fruits and vegetables as oranges and tomatoes if the protective rind and the cell membranes are not ruptured. Storage, bruising, handling, and crushing of many of the vegetables and fruits greatly reduce their vitamin C content. This trauma causes the liberation of enzymes (oxidases) which in the

presence of air catalyze the oxidation of ascorbic acid (Kertesz²¹ et al 1936; Johnson et al²² 1937). This is a rapid reaction and may lead to complete inactivation of the injured tissue in a few minutes. Modern cold storage and canning, if properly performed, affect the vitamin C content relatively little. Even if kept at ice box temperatures, canned foods if allowed to stand after opening will result in considerable destruction of the vitamin C content. Long stewing or boiling, cooking in open containers or containers made of copper (the presence of air and the merest traces of copper lead to complete inactivation often in a few minutes), over salting and the use of soda all tend to increase the loss of this important vitamin. The addition of soda to cooking vegetables may produce a better color but will lead to increased loss of vitamin C. In general, vitamin C is less subject to oxidation in those fruits and vegetables which are acid. Baked and boiled potatoes are reported (Wood²³ 1935) to show only small losses unless overcooked. Fruit jellies and jams are usually low in vitamin C. Warmed over foods are practically free from this vitamin. There is a growing tendency to omit foods which have a high ascorbic acid content. An analysis of the diet of 50 patients was made at the Thewlis Clinic at Wakefield¹², R. I. Their report showed that 18 per cent were taking over 500 mg. of vitamin C per week. 10 per cent of the diets contained no vitamin C. 34 per cent were taking less than 200 mg. per week. Since this vitamin cannot be supplied from within, and since there is no appreciable store in the body it is little wonder that we are easy 'prey' for the virus and other bacteria.

The requirements of vitamin C depend not only on weight but also on metabolic activity in which growth plays a large part. Poor hygiene, overcrowding, dampness, cold and physical work (which includes play) favor the development of a shortage. The relatively small store of ascorbic acid maintained by the body even under good conditions, the relatively narrow margin between health and pathological changes and the evidence of a considerable incidence of hypovitaminosis C combine to emphasize the importance of prevention by an adequate dietary. Parents must learn that commercial orange drinks which do not contain freshly prepared orange juice are practically free from ascorbic acid. The trend must be away from the carbonated soft drinks and back to the 'old fashion' days of citrus fruit juices. If parents will make their children drink as many glasses of citrus fruit juice each day as they now allow them bottle's of carbonated drinks, Polio and disease in general will rapidly assume a less important role in our lives.

SUMMARY

Vitamin C possesses abilities which are characterized by its capacity to antagonize many of the pharmacological effects of histamine. It should be employed with the antihistamine drugs in all allergic states. It is because of this factor that it serves so well in the treatment of acute rheumatic fever. Aside from this and the virus diseases it is of tremendous value in all diseases in which an exotoxin is produced. It also has a specificity for SNAKE BITE except for the cobra and the coral. It neutralizes all exotoxins. It is directly concerned with antibody formation and this in turn leads to an increase in gamma globulin of the blood serum. It joins with the virus to form a new compound which is destroyed by oxidation. It makes all body cells more permeable which allows entrance of immune factors otherwise denied. It prevents or lessens tissue damage. It serves as a hydrogen

transport in cellular respiration. It functions as a dehydrator and diuretic. It is the KEY to good health. Don't lose THIS key for it might lock or unlock your life.

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This is Dr. Fred Klenner's major review article on the use of vitamin C in his medical practice, emphasizing the use of massive injections of the vitamin in treating a variety of diseases and health threats. Diseases and other health threats whose treatment involved the use of injections of vitamin C include pneumonia; bacillary dysentery; severe burns; carbon monoxide poisoning; obstetrics; toxins produced by snakes, flying insects, spiders, caterpillars, and certain plants; mononucleosis; barbiturate poisoning; lockjaw; trichinosis; hepatitis; viral pancarditis; chicken pox; alcohol intoxication; complications of smallpox vaccination; virus encephalitis; surgery; scarlet fever; pesticide poisoning; nasal diphtheria; polio; and repeating virus infections with influenza-like symptoms. "Ascorbic acid," he says, "must be given by needle to bring about quick reversal of various 'insults' to the human body." Injection size ranges from 350 mg to 1200 mg of vitamin C per Kg body weight. Data on injection schedule are provided.—*R.D.M.*

Observations on the Dose and Administration of Ascorbic Acid When Employed Beyond the Range of a Vitamin in Human Pathology

Frederick R. Klenner, M.D., F.C.C.P.

Journal of Applied Nutrition, 1971, Vol. 23, Nos. 3 and 4, pp. 61–87.

Editors Note:

Because of the unusually high amounts of ascorbic acid used in Dr. Klenner's treatment, as reported in his paper, we asked him to verify amounts mentioned. Following is his answer:



"To the Editor of the ICAN Journal: This will confirm that all 'quantity' factors given in my paper are correct and can be confirmed from hospital and medical office records. The notation relative to 150 grams represents the amount used for reversing pathology in a given case and was the amount given over a period of 24 hours. (The I.V. was continuous.) This was given in three bottles of 5D water, decanting only enough from 1000 c.c. to be replaced by the 'C' ampules.

"Recently the FDA has published a 'warning' that too much soda-ascorbate might be harmful, referring to the sodium ion. In reply to this I can state that for many years I have taken 10 to 20 grams of sodium ascorbate by mouth daily, and my blood sodium remains normal. These levels are checked by an approved laboratory. 20 grams each day and my urine remains at or just above pH 6."

Signed:
Fred R. Klenner, M.D.

ANCIENT HISTORY AND HOMESPUN VITAMIN C THERAPYS

Folklore of past civilizations report that for every disease afflicting man there is an herb or its equivalent that will effect a cure. In Puerto Rico the story has long been told "that to have the health tree Acerola in one's back yard would keep colds out of the front door."¹ The ascorbic acid content of this cherry-like fruit is thirty times that found in oranges. In Pennsylvania, U.S.A., it was, and for many still is, Boneset, scientifically called *Eupatorium perfoliatum*.² Although it is now rarely prescribed by physicians, Boneset was the most commonly used medicinal plant of eastern United States. Most farmsteads had a bundle of dried Boneset in the attic or woodshed from which a most bitter tea would be meted out to the unfortunate victim of a cold or fever. Having lived in that section of the country we qualified many times for this particular drink. The Flu of 1918 stands out very forcefully in that the Klenners survived when scores about us were dying. Although bitter it was curative and most of the time the cure was overnight. Several years ago my curiosity led me to assay this "herbal medicine" and to my surprise and delight I found that we had been taking from ten to thirty grams of natural vitamin C at one time. Even then it was given by body weight. Children one cupful; adults two to three cupfuls. Cups those days held eight ounces. Twentieth century man seemingly forgets that his ancestors made crude drugs from various plants and roots, and that these decoctions, infusions, juices, powders, pills and ointments served his purpose. Elegant pharmacy has only made the forms and shapes more acceptable.

Early specifications, action and dosages for administrations

To understand the chemical behavior of ascorbic acid in human pathology, one must go beyond its present academic status either as a factor essential for life or as a substance necessary to prevent scurvy. This knowledge is elementary. Listen to what appeared in Food and Life Yearbook 1939, U.S. Department of Agriculture:³ "In fact even when there is not a single outward symptom of trouble, a person may be in a state of vitamin C deficiency more dangerous than scurvy itself. When such a condition is not detected, and continues un-corrected, the teeth and bones will be damaged, and what may be even more serious, the blood stream is weakened to the point where it can no longer resist or fight infections not so easily cured as scurvy." It is true that without these infinitesimal amounts myriads of body processes would deteriorate and even come to a fatal halt.

Ascorbic acid has many important functions. It is a powerful oxidizer and when given in massive amounts; that is, 50 grams to 150 grams, intravenously, for certain pathological conditions, and "run in" as fast as 20 Gauge needle will allow, it acts as a "Flash Oxidizer,"⁴ often correcting the pathology within minutes. Ascorbic acid is also a powerful reducing agent. Its neutralizing action on certain toxins, exotoxins, virus infections, endotoxins and histamine is in direct proportion to the amount of the lethal factor involved and the amount of ascorbic acid given. At times it is necessary to use ascorbic acid intramuscularly. It should always be used orally, when possible, along with the needle.

Scurvy historically the target; today's goal of high blood levels to cope with self-induced abuses and physiological traumas

If one is to employ ascorbic acid intelligently, some index for requirements must be realized. Unfortunately there exists today a sort of "brand" called "minimum daily

requirements." This illegitimate "child" has been co-fathered by the National Academy of Science and The National Research Council and represents a tragic error in judgement. There are many factors which increase the demand by the body for ascorbic acid, and unless these are appreciated, at least by physicians, there can be no real progress. It is vitally important that cognizance be taken of the demand by the body for ascorbic acid far beyond so-called scorbutic levels. Briefly these demands can be summarized: 1) The age of the individual; 2) Habits—such as smoking, the use of alcohol, playing habits; 3) Sleep, especially when induced artificially; 4) Trauma—trauma caused by a pathogen, the trauma of work, the trauma of surgery, the trauma to the body produced accidentally or intentionally; 5) Kidney threshold; 6) Environment; 7) Physiological stress; 8) Season of the year; 9) Loss in the stool; 10) Variations in individual absorption; 11) Variations in "binders" in commercial tablets; 12) Body chemistry; 13) Drugs; 14) Pesticides; 15) Body weight; 16) Inadequate storage.

Flexible dosage standards explained as minimal standards

With such knowledge it is no longer possible to accept a set numerical unit in terms of minimal daily requirements. This is true because of the simple fact that people are different and these same people experience different situations at various times. With ascorbic acid, today's adequate supply means little or nothing in terms of the needs for tomorrow. Let us start thinking in terms of maximum requirements. For too long a time we have under supplied our children and ourselves by accepting through negative ignorance and acquiescence so-called standards. Based on scant data on mammalian synthesis, available for the rat, a 70-Kg. individual would produce 1.8 grams⁵ to 4.0 grams⁶ of ascorbic acid per day in the unstressed condition. Under stress, up to 15.2 grams.⁷ Compare this to the 70 mg recommended for daily requirements without stress and 200 mg for the simple stress of the obstetrical patient, and you will recognize the disparity and understand why we have been waging a one man war against the establishment in Washington for 23 years.

Ascorbic acid not synthesized by man

Work on mammalian biosynthesis of ascorbic acid indicates that the vitamin C story as is generally accepted represents an over simplification of available evidence.^{8,9,10} This often leads to misinterpretations and false impressions. It has been proposed that the biochemical lesion which produces the human need for exogenous sources of ascorbic acid, is the absence of the active enzyme, 1-gulonolactone oxidase from the human liver.¹¹ A defect or loss of the gene controlling the synthesis of this enzyme in man, blocks the final phase in the series for converting glucose to ascorbic acid. Virus can mutate cells, X-Rays can do it and it can occur by chance. Such a mutation could have happened, denying all progenies of this mutated animal the ability to produce ascorbic acid. Survival demanded ascorbic acid from an exogenous source. This is not remarkable. Other recognized genetic diseases in which a missing enzyme causes a pathological syndrome, in man, are phenylketonuria, galactosemia and alkaptonuria.

It is worthy to note that Sealock and Goodland have ascribed to ascorbic acid the faculty of being the necessary co-enzyme in the metabolic oxidation of tyrosine. The velocity of the oxidation in this reaction is dependent upon the concentration of vitamin

C. Tyrosine is essential in breaking down protein to usable amino acid. The scorbutic guinea-pig's liver is unable to oxidize tyrosine except in the presence of ascorbic acid. This suggests a lead in the study of the metabolic abnormality—Alkaptonuria—in humans. Ascorbic acid administration will correct the alkaptonuria of the scorbutic guinea pig. Its effect on human alkaptonuria has been inconsistent. The reason: Inadequate use of ascorbic acid.

Bio-chemist Irwin Stone's concept has practical value

The inability of man to manufacture his own ascorbic acid, due to genetic fault, has been called "hypoascorbemia" by Irwin Stone.¹² This is another reason for abolishing the present concept of daily minimal requirements. The physiological requirements in man are no different from other mammals capable of carrying out this synthesis.

Various procedures testing for the vitamin C levels and requirements of the body

Various tests have been employed to determine the degree of body saturation of vitamin C, but for the most part they have been misleading. Blood and urine samples analyzed with 2:6 dichlorophenol indophenol will give values roughly 7 percent less than when testing with dinitrophenol hydrazine. Gothlin advocates the capillary fragility test which is similar to the tourniquet test of Hess in results. Both can be used to estimate the quantity of vitamin C necessary to maintain capillary integrity. The intradermal test of Rotter as modified by Slobody¹³ is again gaining new recruits. In principle it is the same as the lingual test of Ringdorf and Cheraskin¹⁴ since both are based on the time required to decolorize dye. The lingual test is rapid and simple to perform but it requires a syringe with a 25 gauge needle and a stop watch. Since the dye methods depend on the reduction of the reagent by vitamin C, any substance having a reducing potential lower than the dye is a possible source of interference. Twenty years ago we elected to measure, as a therapeutic gauge, the amount of vitamin C in urine by borrowing on its ability to reduce qualitative Benedict's solution. A 2 plus Benedict's reaction in a known dextrose free urine was accepted as a standard. This test was helpful in gauging requirements for simple stress, but not accurate enough when using needle therapy. Fifteen years ago we developed the Silver Nitrate-Urine¹⁵ test. This test employs 10 drops of 5 percent silver nitrate and 10 drops urine which is placed in a Wasserman tube. Read in two minutes it will give a color pattern showing white, beige, smoke gray or charcoal or various combinations of any two depending upon the degree of saturation. We have found this color index test is all one will need for establishing the correct amount of ascorbic acid to use by mouth, by muscle, by vein in the handling of all types of human pathology either as the specific drug or as an adjuvant with other antibiotics or neutralizing chemicals. In severe pathological conditions the urine sample, taken every four hours, must show a fine charcoal-like precipitation with a clear supernatant liquid if positive clinical results are to be realized. Spilling in the urine is not new. Abraham and Keefer have demonstrated that when penicillin is injected intravenously, excretions in the urine account for 60 percent of the administered dose.

*Role played by ascorbic acid in intercellular reactions,
neutralizing, possibly controlling virus production*

In 1935 Stanley isolated a crystalline protein possessing the properties of tobacco mosaic virus. It contained two substances, ribonucleic acid (RNA) and protein. The simple structure characteristic of tobacco mosaic virus was soon found to be a basic property of many human viruses such as coxsackie virus (which I believe to be the cause of Multiple Sclerosis), Echo and polioviruses—they all contain only ribonucleic acid and protein. There exist minor variations. Adenoviruses contain deoxyribonucleic acid (DNA) and protein. Other viruses such as that causing influenza contain added lipid and polysaccharides. Deoxyribonucleic acid is used to program the large viruses, like mumps, ribonucleic acid is used to program the small viruses, like measles. The role of the protein coat is to protect the parasitic but unstable nucleic acid as it rides the “blood highway” or “lymphatic system” to gain specific cell entry. Pure viral nucleic acid without its protein coat can be inactivated by constituents of normal blood. There are several theories as to what happens after cell entry: 1) Once inside a given cell the virus nucleic acid sheds its protein coat and proceeds to modify the host cell by either creating mutations or by directly substituting its own nucleic acid; 2) The infectious nucleic acid, after entering a human cell, retains its protein coat and starts to produce its own type protein coat¹⁶ and viral nucleic acid, so that new units can either depart to enter other cells or by destruction of the cell, thus making the infection more severe; 3) The introduction of a foreign fragment of nucleic acid in the cell-virus interaction approach as postulated by Starr.¹⁷ In the Starr theory there can exist cells with partial chromosome make-up and cells with multi-nuclei. Hiliary Kropowski holds that these partial cells are “pseudo-virions”¹⁸ and are found in some tumor-virus infections. A key factor in the Starr-Kropowski thinking is that the cell maintains its biological integrity to support virus development despite the abnormal morphology and genetic deficiency. If these invaded cells could be destroyed or the invader neutralized the illness would suddenly terminate. Ascorbic acid has the capability of entering all cells. Under normal circumstances its presence is beneficial to the cell, however, when the cell has been invaded by a foreign substance, like virus nucleic acid, enzymic action by ascorbic acid contributes to the breakdown of virus nucleic acid to adenosine deaminase which converts adenosine to inosine. The net result is to lead to purines which are extensively catabolized and not to purines which are utilized for further nucleic acid. Ascorbic acid also joins with the available virus protein, making a new macromolecule which acts as the repressor factor. It has been demonstrated that when combined with the repressor, the operator gene, virus nucleic acid, cannot react with any other substance and cannot induce activity in the structural gene, therefore inhibiting the multiplication of new virus bodies. The tensile strength of the cell membrane is exceeded by these macromolecules with rupture and destruction. Another hypothesis is that vitamin C acts to create new “L” viruses which are impotent. Still another, that the “binding” alone is sufficient to destroy the virus.

*Promptness of massive ascorbic acid in avoiding fatal encephalitis
related to stubborn head and chest colds*

In 1953¹⁹ we presented a case history and films of a patient with virus pneumonia. This patient was unconscious, with a fever of 106.8°F (A. corrected) when admitted to the hospital. 140 grams ascorbic acid was given intravenously over a period of 72 hours at which time she was awake, sitting up in bed and taking fluids freely by mouth. The temperature was normal. Since that time we have observed a more deadly syndrome associated with a virus causing head and chest colds. This is one of the adenovirus striking in the area of the upper respiratory tract with resulting fever, sore throat and eyes, and when in children can cause fatal pneumonia. More often death is indirect by way of incipient encephalitis where the child can be dead in 30 minutes. These are the babies and children found dead in bed and attributed to suffocation. It is suffocation but by way of a syndrome we observed and reported in 1957²⁰ which is similar to that found in cephalic tetanus-toxemia culminating in diaphragmatic spasm, with dyspnea and finally asphyxia.²¹ By 1958²² we had collected sufficient information from our office and hospital patients to catalog this deadly syndrome into two important stages. A 1) There is always a history of having had the "Flu" which lasted 48 to 96 hours complicated with extreme physical or mental distress; 2) A mild cold, similar to an allergic rhinitis, which lingered on for several weeks but did not incapacitate the individual. B This stage, which is always sudden, will present itself in at least seven forms: 1) Convulsive seizures; 2) Extreme excitability resembling delirium tremens if an adult and with dancing of the eyeballs if a child; 3) Severe chill; 4) Strangling in the course of eating or drinking (bulbar type); 5) Collapse; 6) Stupor; 7) Hemiplegic type.

SECOND STAGE FINDINGS

Other findings of this dramatic second stage are: 1) Rapid pulse; 2) Temperature can be normal, moderately elevated or high; 3) Respirations twice to three times normal and in some cases will be suggestive of air hunger; 4) Pupils will be moderately open and in some instances (hemiplegic) one will be markedly dilated; 5) Urine negative; 6) The white blood count running from 6000 to 25,000 with a high poly count in the differential; 7) Young patients starting the second phase with a convulsion there has been not only a history of normal bowel movements but also an enema given at the time of first examination has produced a normal stool; 8) Bladder spincted control was abnormal in our cases who convulsed or who were in coma.

NEUROLOGICAL CHANGES

It is apparent that the second stage of this syndrome is triggered by a breakthrough at the site of the blood-brain barrier. The time required for neurological changes to become evident is roughly comparable to the time necessary for similar neuropathology to be demonstrated following a severe head injury. Cerebral edema exists in both conditions. In my practice I start massive ascorbic acid therapy immediately. I have seen children dead in from 30 minutes to 2 hours because their attending physician was not impressed with their illness upon hospital admission. An autopsy on one of these

patients showed bi-lateral pneumonitis—all one needs to spark a deadly encephalitis. To indicate just how common this syndrome presents itself, I relate here a newspaper account of a 15 year old girl who had a mild, lingering cold for several weeks. She attended a dance party one evening and except for a complaint of feeling extremely tired, she went to bed apparently well. She was found dead in bed the following morning. An autopsy showed bi-lateral pneumonia. How many times have you read such an account? This is why it is necessary for everybody to take adequate supplemental vitamin C to guard against such disasters.

LITERATURE RESEARCH

In 1960 we decided to re-search the literature before writing our paper, "Virus Encephalitis As A Sequel Of The Pneumonias."²² Rosenfield in 1903 described a similar syndrome under the caption "Brain Purpura or Haemorrhagic Encephalitis." Comby, in 1907, was the first to call attention to the interesting "metastatic" sequela of the pneumonias. Baker and Noran in 1945²³ enumerated five groups, each showing certain definite clinical characteristics which may be of both diagnostic and prognostic significance in relation to this virus syndrome. 1) Symptoms of a nonspecific nature—headache, vomiting, irritability; 2) Delirious type; 3) Convulsive type; 4) Lethargic type; 5) Hemiplegic type. These groups plus two additional types, namely: 6) Chill—blood invasion type; 7) Collapse, were as we reported them, independently, in the Tri-State Medical Journal, October 1958. Their results: Some recovered, some died and still others lived as "vegetation"—mental cripples. All of our patients recovered. Thirteen years from the time of the Baker-Noran report to the time of our report and 13 years from the time of our report to the present time. This makes the issue urgent. Physicians must recognize the inherent danger of the lingering head or chest cold and appreciate the importance of early massive vitamin C therapy.

How does the brain become involved in encephalitis?—some speculations

Clinical problems such as these groups present, leads one to speculate on the pathways in which the virus gains entrance into the brain. We can summarize: 1) Through the olfactory nerves; 2) Through the portals of the stomach from material swallowed, either pulmonary or upper respiratory drainage; 3) Direct extension from otitis media or from mastoid cells; 4) The blood stream. Arriving in the brain the virus goes through the blood cerebro spinal fluid barrier and/or the blood brain barrier by one of three ways: a) Electrical charge; b) Chemical lysis of tissue; c) Osmosis. Bakay²⁴ reported that the permeability of the blood-brain barrier can be changed by introducing various toxic agents into the blood circulation. Chambers and Zweifach²⁵ emphasized the importance of the intercellular cement of the capillary wall in regulating permeability of the blood vessels of the central nervous system. In this syndrome the toxic substance is an adenovirus. Ascorbic acid will repair and maintain the integrity of the capillary wall.

Burns—degrees explained and some therapy rational

In the treatment of burns ascorbic acid, in sufficient amounts, reflects itself as a truly miracle substance. In the early forties, when I was using ascorbic acid, intramuscularly,

in treating bacillary dysentery, shiga type, with excellent results, Lund, Lam and many others were using, what they called, massive doses of ascorbic acid in the treatment of burns. One or two grams each day, in fluids, was the recognized dose. Burns are at the beginning first degree and some remain as just an erythema. Many times the first degree burn progresses rapidly to the second degree stage and remains as "blisters". Still others go on to third degree which usually is more pronounced on the third plus post burn day. There is a fourth stage which results from lack of knowledge in treatment. It terminates with skin grafting and plastic surgery. We believe that ascorbic acid will eliminate the fourth stage and the third stage if used as we will later program.

Burns—continued descriptive and related therapies

The pathologic physiology of a burn wound from the moment of the accident is in a state of dynamic change until the wound heals or the patient dies. The primary consideration is the phenomenon of blood sludging originally recognized by Knisely in 1945.^{26,27} Initially there is intravascular agglutination of red blood cells into distinctly visible, smooth, hard, rigid, basic masses. Lofstrom in 1959 demonstrated that the oxygen uptake by the tissues is greatly reduced because of the sludging and therefore reduced rate of flow. Berkeley²⁸ in 1960 concluded that this phenomenon of sludging or agglutination results in capillary thrombosis in the area of the burn, extending proximally to involve the large arterioles and venules and thereby creating tissue destruction greater than that originally produced by the burn. Anoxia produces added tissue destruction. Lund and Levenson²⁹ found that after severe burns there is considerable alteration in the metabolism of ascorbic acid as shown by a low concentration of ascorbic acid in the plasma either with the patient fasting or after saturation tests and also low urinary excretion of vitamin C either with the patient fasting or after the injection of test doses. The extent of the abnormality closely paralleled the severity of the burn. Bergman³⁰ reported an increase demand for ascorbic acid in burns especially when epithelization and formation of granulation tissue are taking place. Lam³¹ also reported in 1941 a marked decrease in the plasma ascorbic acid concentration in patients with severe burns. Klasson³² although limiting the amount of ascorbic acid to a dose range of 300mg to 2000mg daily, in divided doses, found that it hastened the healing of wounds by producing healthy granulation tissue and also that it reduced local edema. He rationalized that ascorbic acid used locally as a 2% dressing possessed astringent properties similar to hydrogen peroxide. He also reported that antibiotic therapy was rarely necessary.

Severe burns and related therapy

Harlen Stone³³ suggested the use of gentamicin in major burns to lower the sepsis caused by pseudomonas. Absorption of its exotoxin from the infected burn wound inhibits the bacterial defense mechanism of the reticuloendothelial system. Death can result either from the toxemia alone or from an associated septicemia. We have found that the secret in treating burns can be summarized in five steps: 1) The use of the "old covered wagon" type cradle when indicated, with three 25 watt bulbs. The patient controls the heat by turning on and off the first bulb as needed to keep warm. No garments or dressings are allowed; 2) The employment of a 3% ascorbic acid solution as a spray over the entire area of the burn. The spray can be applied with a Devilbis unit

using an ordinary portable pressure pump. The old type "flit gun" can also be used or even a 50 c.c. syringe with a 20 gauge needle. The 3% solution is used every 2 to 4 hours for a period of roughly five days; 3) The use of vitamin A and D ointment over the area of the burn and this is now alternated, q4h with the 3% ascorbic acid solution; 4) The administration of massive doses of ascorbic acid by vein and by mouth. 500 mg per Kg. body weight diluted to at least 18 c.c. per gram vitamin C using 5% dextrose in water, saline in water or Ringers solution and for the initial injection, run in as fast as a 20 gauge needle or catheter will carry the flow. Cut-downs are frequently necessary and the foot-ankle area is recommended. Vitamin C solution is repeated every 8 hours for the first several days, then at 12 hour intervals. Ascorbic acid, by mouth, is given to tolerance. Loose stools is accepted as this index. Using large doses of ascorbic acid I.V. will necessitate the administration of at least one gram calcium gluconate, daily, to replace free calcium ions removed in the breakdown chemical action as ascorbic acid goes to dehydroascorbic acid, then to ketogulonic acid and later to oxalic acid³⁴ as the calcium salt; 5) Supportative treatment; that is, whole blood and maintaining electrolyte balance. If seen early after the burn there will be no infections and no eschar formations. This eliminates fluid formation, since the eschar traps will not exist and there will be no distal edema because the venous and lymphatic systems will remain open. There will be no arterial obstruction and no nerve compression. Pseudomonas will not be a problem, since ascorbic acid destroys the exotoxin systemically and locally. Even if the burn is seen late when pseudomonas is a major problem the gram negative bacilli will be destroyed in a few days leaving a clean healthy surface. I have seen eschars 2 inches wide and ½ inch thick, severely infected so that stench had to be controlled with deodorizing sprays, melt away when employing the method outlined. Ascorbic acid also eliminates pain so that opiates or their equivalent are not required. In extremely extensive burns that involve back and front of the patient, the "Hoverbed"³⁵ employed by the British should be considered. It uses the same principle as the hovercraft to lift a solid object. What has been overlooked in burns is that there are many living epithelial cells in the areas that grossly look like "raw muscle." With the use of ascorbic acid these cells are kept viable, will multiply and soon meet with other proliferating units in the establishment of a new integument.

Regarding personal and environmental pollution—carbon monoxide

We are all plagued with varying degrees of chronic carbon monoxide poisoning. This is the price we pay for putting our "railroads" on our highways, smoking and being too lazy to walk. Small amounts of carbon monoxide, if constantly maintained in the alveoli, can produce serious effects. Carbon monoxide in the inspired air leads to oxygen deficiency in the tissues causing extreme exhaustion. The affinity of carbon monoxide for hemoglobin is roughly 300 times as great as that for oxygen. In addition to active replacement of oxy-hemoglobin the presence of some proportion of carboxy-hemoglobin decreases the dissociability of such oxy-hemoglobin as remains. Carbon monoxide can be released from hemoglobin if the patient is exposed to high pressure of oxygen, 93% along with 7% carbon dioxide. This is not always available. Ascorbic acid in the blood is constantly losing molecules of water. Perfectly dry carbon monoxide and oxygen cannot unite to form carbon dioxide, but carbon monoxide and water may give rise to carbon

dioxide in the complete absence of oxygen. The reactions which take place are $\text{CO} + \text{H}_2\text{O} = \text{HCOOH} \text{ CO}_2 + \text{H}_2$ (Wright). Here the oxygen of the water has been used to oxidize carbon monoxide to carbon dioxide with the liberation of hydrogen. Glutathione may facilitate this cellular oxidation by acting as a hydrogen acceptor (Hopkins). Clinical experience suggests that if sufficient ascorbic acid is suddenly placed into the blood stream—12 grams to 50 grams—that through “Flash Oxidation” a concentration of oxygen is made high enough to pull carbon monoxide from hemoglobin to form carbon dioxide. This rapidly formed carbon dioxide acts with the high oxygen tension to serve the same purpose as when given by “mask,” further enhancing the chemical action taking place. Ascorbic acid will also prevent residuals such as paralysis, blindness, interference with sensations, muscle spasms or twitchings which in some cases can be permanent.

Primary and lasting benefits in pregnancy

Observations made on over 300 consecutive obstetrical cases using supplemental ascorbic acid, by mouth, convinced me that failure to use this agent in sufficient amounts in pregnancy borders on malpractice. The lowest amount of ascorbic acid used was 4 grams and the highest amount 15 grams each day. (Remember the rat-no stress manufactures equivalent “C” up to 4 grams and with stress up to 15.2 grams). Requirements were roughly 4 grams first trimester, 6 grams second trimester and 10 grams third trimester. Approximately 20 percent required 15 grams, each day, during last trimester. Eighty percent of this series received a booster injection of 10 grams, intravenously, on admission to the hospital. Hemoglobin levels were much easier to maintain. Leg cramps were less than three percent and always was associated with “getting out” of Vitamin C tablets. Striae gravidarum was seldom encountered and when it was present there existed an associated problem of too much eating and too little walking. The capacity of the skin to resist the pressure of an expanding uterus will also vary in different individuals. Labor was shorter and less painful. There were no postpartum hemorrhages. The perineum was found to be remarkably elastic and episiotomy was performed electively. Healing was always by first intention and even after 15 and 20 years following the last child the firmness of the perineum is found to be similar to that of a primigravida in those who have continued their daily supplemental vitamin C. No patient required catheterization. No toxic manifestations were demonstrated in this series. There was no cardiac stress even though 22 patients of the series had rheumatic hearts. One patient in particular was carried through two pregnancies without complications. She had been warned by her previous obstetrician that a second pregnancy would terminate with a maternal death. She received no ascorbic acid with her first pregnancy. This lady has been back teaching school for the past 10 years. She still takes 10 grams of ascorbic acid daily. Infants born under massive ascorbic acid therapy were all robust. Not a single case required resuscitation. We experienced no feeding problems. The Fultz quadruplets were in this series. They took milk nourishment on the second day. These babies were started on 50 mg ascorbic acid the first day and, of course, this was increased as time went on. Our only nursery equipment was one hospital bed, an old, used single unit hot plate and an equally old 10 quart kettle. Humidity and ascorbic acid tells this story. They are the only quadruplets that have survived in southeastern United States.

Another case of which I am justly proud is one in which we delivered 10 children to one couple. All are healthy and good looking. There were no miscarriages. All are living and well. They are frequently referred to as the vitamin C kids, in fact all of the babies from this series were called "Vitamin C Babies" by the nursing personnel—they were distinctly different.

*How concerned should we be about oxalic acid and kidney stones?
A technical explanation*

One of the "scare" weapons used by the critics on high daily doses of ascorbic acid is the oxalic acid-kidney stone hypothesis. Meakins³⁶ states that the chief factors in the formation of renal calculi are perversions of metabolic processes, infection and stasis in the urinary tract. There are two schools of thought on stone formation: 1) That there is a central nucleus of colloids on which the crystalloids are precipitated; 2) That the crystalloids are deposited from the urine in which they are present in concentrated solution, in which salt and hydrogen ion concentrations are important factors. In all cases stasis and a concentrated urine appear to be the chief physiological factors. The only way that oxalic acid can be produced from ascorbic acid is through splitting of the lactone ring. This happens above pH5. The reaction of urine when 10 grams of vitamin C is taken daily is usually pH6. Oxalic acid precipitates out of solution only from a neutral or alkaline solution—pH7 to pH10. Kelli and Zilva³⁷ reported that "Nutrition experiments showed that dehydroascorbic acid is protected in vivo from rapid transformation to the antiscorbutically impotent diketogulonic acid from which oxalic acid is derived. Values reported in the literature for normal 24 hour urinary oxalate excretions for humans range from 14 mg to 56 mg. Lamden et al.³⁸ found in a group of volunteers that the ingestion of 9 grams ascorbic acid daily resulted in oxalate spills as high as 68 mg for 24 hours and in the controls without extra vitamin C the high was 64 mg for a 24 hour period. These critics have overlooked the individual with diabetes mellitus. The amount of oxalic acid found in the diabetic patient approximates that found in the urine of a normal person taking 10 grams vitamin C each day. With the diabetic we find a paradox. Give this individual 10 grams ascorbic acid daily, by mouth, and the urinary oxalate excretion remains relatively unchanged. Diabetics are known for their diuresis. The individual who takes 10 or more grams of vitamin C each day will find that this organic compound is an excellent diuretic. No urinary stasis; no urine concentration. The ascorbic acid-kidney stone story is a myth. Methylene blue will dissolve calcium oxalate stones giving 65 mg orally 2 to 3 times a day. (Dr. M. J. Vernon Smith: Med. World News, Dec. 4, 1970)

Why death from insect and snake bites?

It is estimated that 6500 deaths occur each year in the United States from snake bite. Many more from various flying insects, spiders, certain plants and some caterpillars. These are needless deaths. Several factors are at work in these pathologies: 1) The tox-albumin of the snake bite, like the copperhead or rattler; 2) Formic acid plus a toxin with a protein cover, called proteotoxin by Arthus,³⁹ such as found in bees and wasps; 3) Neurotoxin from the Black Widow, the Fiddle Spider and snakes like the Cobra and

Coral; 4) Production of histamine, especially in the more severe stings and bites. Wells⁴⁰ in 1925 called the poison of certain spiders and snakes zootoxins and of poisonous plants, phytotoxins. Ford⁴¹ in 1911 reported three classes of toxins in plants and fungi: 1) Nerve poisons—muscarine; 2) Those causing structural changes in the viscera with resulting fatty degeneration; 3) Gastrointestinal irritants.

Ascorbic acid to the rescue

It is a demonstrated principle that the production of histamine and other end products from deaminized cell proteins released by injury to cells are a cause of shock. The clinical value of ascorbic acid in combating shock is explained when we realize that the deaminizing enzymes from the damaged cells are inhibited by vitamin C.⁴² It has been shown by Chambers and Pollock⁴³ that mechanical damage to a cell results in pH changes which reverse the cell enzymes from constructive to destructive activity. The pH changes spread to other cells. This destructive activity releases histamine a major shock producing substance. The presence of vitamin C inhibits this enzyme transition into the destructive phase. Clark and Rossiter⁴⁴ reported that conditions of shock and stress cause depletion of the ascorbic acid content of the plasma. As with the virus bodies, ascorbic acid also joins with the protein factor of these toxins effecting quick destruction. The answer to these emergencies is simple. Large amounts of ascorbic acid 350 mg to 700 mg per Kg. body weight given intravenously. In small patients, where veins are at a premium, ascorbic acid can easily be given intramuscularly in amounts up to two grams at one site. Several areas can be used with each dose given. Ice held to the gluteal muscles until red, almost eliminates the pain. We always reapply the ice for a few minutes after the injection. Ascorbic acid is also given, by mouth, as followup treatment. Every emergency room should be stocked with vitamin C ampoules of sufficient strength so that time will never be counted—as a factor in saving a life. The 4 gram, 20 c.c. ampoule and 10 gram 50 c.c. ampoule must be made available to the physician.

A case history—success due to promptness with a twelve gram injection

As an example of the lethal effect of certain stings and bites, I briefly relate a case history. An adult male came to my office complaining of severe chest pain and the inability to take a deep breath. Stated that he had been “stung” or “bitten” 10 minutes earlier. Thinking that it was a Black Widow and not bothering to look for fang marks, due to the gravity of the situation, I gave one gram calcium gluconate intravenously. This gave no relief. He begged for help saying he was dying. He was becoming cyanotic. Twelve grams of vitamin C was quickly pulled into a 50 c.c. syringe and with a 20 gauge needle was given intravenously as fast as the plunger could be pushed. Even before the injection was completed, he exclaimed, “Thank God”. The poison had been neutralized that rapidly. He was sent home to locate the “culprit”. He soon returned with an object that looked like a mouse. It was 1½ inches long with long brown hair. There was a dark ridge down the entire back. It had seven pairs of propelling units and a tail much like a mouse. The following day I took “The Thing” to Duke University where it was identified as the Puss Caterpillar. This unusual caterpillar left 44 red raised marks on the back of its victim. Except for vitamin C this individual would have died from shock and asphyxiation.

Some concern answered regarding high dosage of ascorbic acid

Merton Lamden, a bio-chemist, writing in the New England Journal of Medicine, Feb. 11, 1971, expresses grave doubts about the safety of large doses of ascorbic acid taken by mouth. He gives a report by Paterson⁴⁵ on the diabetogenic effect of dehydroascorbic acid on rats. Paterson in 1950 employed only the Ketone formula of ascorbic acid, dehydroascorbic acid, which he administered, undiluted, intravenously, in extraordinary amounts. His results were based on giving rats, weighing 100 grams to 120 grams, dehydroascorbic acid in doses from 20 to 50 mg. This transposed to a man weighing 70 kilograms would represent a dose of 3,500 grams—roughly 5,000 grams ascorbic acid. Obviously the work has no relationship with the ingestion of ascorbic acid by humans. I have taken from 10 to 20 grams of ascorbic acid daily since my last visit to this college—18 years ago. I do not have diabetes mellitus and if I might digress a moment, neither have I had a kidney stone.

Diabetes mellitus response to 10 grams ascorbic acid by mouth

Over the past 17 years we have studied the effect of 10 grams, by mouth, in patients with diabetes mellitus. We found that every diabetic not taking supplemental vitamin C could be classified as having sub-clinical scurvy. For this reason they find it difficult to heal wounds. The diabetic patient will use the supplemental vitamin C for better utilization of his insulin. It will assist the liver in the metabolism of carbohydrates and to re-instate his body to heal wounds like normal individuals. We found that 60% of all diabetics could be controlled with diet and 10 grams ascorbic acid daily. The other 40% will need much less needle insulin and less oral medication. Contrary to what Medical News Letter, (Vol. 12 #26, Dec. 25, 1970) carried to the physicians the Tes-Tape is accurate in testing urine samples.

Observations following post-surgery cases on blood plasma levels of ascorbic acid. Deduction is evident of the need for substantial amounts of ascorbic acid prior to surgery

In 1960 and again in 1966, in papers delivered before the Tri-State Medical Society, I called attention to the “scurvy” levels of ascorbic acid found in postoperative patients. Plasma levels recorded before starting anesthesia and after cessation of such inhalants and completion of surgery remained unchanged. This has lead many to believe that surgery created little or no demand for supplemental “C”. We found, however, that samples of blood taken six hours after surgery showed drops of approximately $\frac{1}{4}$ the starting amount and at 12 hours the levels were down to one-half. Samples taken 24 hours later, without added ascorbic acid to fluids, showed levels $\frac{3}{4}$ lower than the original samples. Baylor University re-search team reported similar findings in 1965. Bartlett, Jones⁴⁶ and others reported that in spite of low levels of plasma ascorbic acid at time of surgery, normal wound healing may be produced by adequate vitamin C therapy during the post-operative period. Lanman and Ingalls⁴⁷ showed that the tensile strength of healing wounds is lowered in the presence of “scurvy plasma levels”. Schumacher⁴⁸ reported that the pre-operative use of as little as 500 mg of vitamin C given orally “was remarkably successful in preventing shock and weakness” following dental extractions. Many other investigators have shown in both laboratory and clinical

studies, that optimal primary wound healing is dependent to a large extent upon the vitamin C content of the tissues. In 1949, it was my privilege to assist at an abdominal exploratory laparotomy. A mass of small viscera was found "glued together". The area was so friable that every attempt at separation produced a torn intestine. After repairing some 20 tears the surgeon closed the cavity as a hopeless situation. Two grams ascorbic acid was given by syringe every two hours for 48 hours and then 4 times each day. In 36 hours the patient was walking the halls and in seven days was discharged with normal elimination and no pain. She has outlived her surgeon by many years. We recommend that all patients take 10 grams ascorbic acid each day. Where this is not done and the surgery is elective, then 10 grams by mouth should be given for several weeks prior to surgery. At least 30 grams should be given, daily, in solutions, post-operatively, until oral medication is allowed and tolerated.

Mononucleosis aided by ascorbic acid

After studying hundreds of college students, Yale researchers have evidence that strengthens the link between mononucleosis and EB virus,⁴⁹ a herpes-like agent also associated with Burkitt lymphoma. Large doses of intravenous "C" has a striking influence on the course of mononucleosis. In one patient who was given the last rites of her church, the girl's mother took things into her own hands when the attending physician refused to give ascorbic acid. In each bottle of intravenous fluids she would quickly "tap in" 20 to 30 grams vitamin C. The patient made an uneventful recovery. Her mother has her B.S. in Nursing and has been a long time advocate of massive "C" therapy.

Could ascorbic acid have anti-cancer features?

Schlegel⁵⁰ from Tulane University has been using 1.5 grams ascorbic acid daily to prevent recurrences of cancer of the bladder. He and biochemist Pipkin have been able to demonstrate that in the presence of ascorbic acid, carcinogenic metabolites will not develop in the urine. They suggest that spontaneous tumor formation is the result of faulty tryptophane metabolism while urine is retained in the bladder. Schlegel termed ascorbic acid "An Anticancer Vitamin". Along this line Glick and Hosoda⁵¹ reported on work by Von Numers and Pettersson that the depletion of mast cells from guinea pigs skin was due to ascorbic acid deficiency. The possibilities indicated are that vitamin C is necessary either directly or indirectly for formation of mast cells, or for their maintenance once formed or both. Ascorbic acid will control myelocytic leukemia provided 25 to 30 grams are taken orally each day. One can only speculate on what massive therapy would do in all forms of cancer. Many pathologic conditions are cured by giving 5 million to 100,000 million units of penicillin as an intravenous drip over a period of 4 to 6 weeks. How long must we wait for someone to start continuous ascorbic acid drip for 2 to 3 months, giving 100 to 300 grams each day, for various malignant conditions?

Barbiturate patients in shock normalized with ascorbic acid

Clemmesen⁵² states that the important principles in management of barbiturate poisoning are anti-shock therapy, continuous oxygen and patent airways. Hadden et al.⁵³ suggest six measures as supportive treatment. An intensive care unit would be necessary to carry out these functions. All one really need do is give adequate ascorbic

acid therapy. One patient who had taken 2640 mg Lotusate (talbutal) was seen in the emergency room with a blood pressure of 60/0. Twelve grams vitamin C was given intravenously with a 50 c.c. syringe and then the needle attached to a bottle of 5D water containing 50 grams ascorbic acid. Within 10 minutes the blood pressure was 100/60 demonstrating the effect of vitamin C on shock. A second bottle of 250 c.c. 5D water containing one gram emivan was started in the other arm. The patient was awake in 3 hours, taking juice with "C" added. She received 125 grams ascorbic acid by vein in 12 hours. Ascorbic acid not only assists with hepatic metabolism but also as a major diuretic flushes these compounds out by way of the kidneys. Nasal oxygen running 6 liters per minute was also employed. Another patient who had masked 2400 mg seconal with paraldehyde was awake after 42 grams of ascorbic acid had been given by vein as fast as a 20 gauge needle could carry the flow. She received 75 grams vitamin C by vein and 30 grams by mouth in a 24 hour period.

Cholesterol not a problem, when daily intake of ascorbic acid is high

Mention should be made of the role⁵⁴ played by vitamin C as a regulator of the rate at which cholesterol is formed in the body; deficiency of the vitamin speeding the formation of this substance. In experimental work, guinea pigs fed a diet free of ascorbic acid showed a 600 percent acceleration in cholesterol formation in the adrenal glands. Ten grams or more each day and then eat all the eggs you want. That is my schedule and my cholesterol remains normal. Russia has published many articles demonstrating these same benefits.

Lock-jaw relieved

Ascorbic acid has no equal as an adjuvant with other drugs in many conditions. With Tolserol it is curative in the treatment of Lockjaw. Both drugs must be used in proper amounts. In our case 1000 mg Tolserol given intravenously to a boy weighing 20 Kg. was the optimal amount to use. In 48 hours he was given 90 grams ascorbic acid and 3000 mg Tolserol, all intravenously.⁵⁵ Jungeblut⁵⁶ reported that vitamin C, when added to tetanus toxin "in vitro", brings about inactivation of the toxin. Two cases of Trichinosis was treated and cured using Vitamin C and Para-Aminobenzoic acid.⁵⁷ Although the temperature curve was returned to normal in 36 hours it was found that nine days of treatment was necessary for permanent cures.

Infectious hepatitis relieved

Viral hepatitis needs brief mentioning. There are two types: 1) Infectious hepatitis; 2) Needle hepatitis. Physical activity has always been considered to increase the severity and prolong the course of the disease.⁵⁸ In Vietnam, Freebern and Repsher showed that pick-and-shovel details had no effects on the 199 controls as against 199 kept at bed rest.⁵⁹ One thing is certain. Given massive intravenous ascorbic acid therapy and patients are well and back to work in from 3 to 7 days. In these cases the vitamin is also employed by mouth as follow-up therapy. Dr. Bauer at the University Clinic, Basel, Switzerland, reported that just 10 grams daily, intravenously, proved the best treatment available.

Ascorbic acid therapy applied to various maladies

We could continue indefinitely extolling the merits of ascorbic acid. Boyd and Campbell⁶⁰ reported excellent results in the healing of corneal ulcers even though their massive doses was 1.5 grams daily. In one case of a corneal burn from the phosphorus off an old time match, the pain was relieved immediately with the intravenous injection of 12 grams vitamin C with a 50 c.c syringe. One gram was prescribed each hour for 50 grams. The cornea was normal in less than 24 hours. One single injection of ascorbic acid calculated at 500 mg per Kg. body weight will reverse heat stroke and one to three injections of the vitamin in a dose range of 400 mg Kg. body weight will effect a dramatic cure in Virus Pancarditis. One gram taken every one to two hours during exposure will prevent sunburn and intravenous injections will quickly relieve the pain and erathema, even the second degree burns when precautions are not taken. One to three injections of 400 mg per Kg. given every eight hours will "dry up" chicken-pox in 24 hours. If nausea is present it will stop the nausea. These injections are usually given with a syringe in a dilution of one gram to 5 c.c fluid. This concentration will produce immediate thirst. This is prevented by having the patient drink a glass of juice just before giving the injection. Forty grams ascorbic acid by vein and 1000 mg to 2000 mg vitamin B-1 intramuscularly will neutralize the person intoxicated by alcohol and will save the life if one drinks after using Antibuse. 5 per cent ointment using a water soluble base will cure acute fever blisters if applied 10 or more times a day and we have removed several small basal cell epitheliomas with a 30 percent ointment. Dr. Virno⁶¹ at the eye clinic, University of Rome, Italy, reported very promising results in glaucoma with a dose schedule of 100 mg per Kg. body weight taken after meals and bed hour. He also reported that these large doses have proved to be safe. In arthritis at least 10 grams daily and those taking 15 to 25 grams daily will experience commensurate benefit. Supportive treatment must also be given. Repair of collagenous tissue is dependent of adequate ascorbic acid. Complications of smallpox vaccination are usually handled by adequate oral ascorbic acid. Several times we found it necessary to give the "C" intravenously along with Adenosine. Twenty percent ichthammol used locally with vaccinia necrosum is good psychology. In herpes zoster two grams vitamin C intramuscularly and 50 mg Adenosine 5-Monophosphoric acid, aqueous solution, also intramuscularly every 12 hours. Compound tincture benzoin locally is helpful. In massive "shingles" ascorbic acid should also be given by vein. Always as much by mouth as can be tolerated. Heavy metal intoxication is also resolved with adequate vitamin C therapy.

General all around benefits via one to ten grams ascorbic acid per day

It has been suggested that ascorbic acid metabolism may be an index of total metabolism and thus serve as a general diagnostic guide. Adults taking at least 10 grams of ascorbic acid daily, and children under ten at least one gram for each year of life will find that the brain will be clearer, the mind more active, the body less wearied and the memory more retentive.

SUMMARY

The types of pathology treated with massive doses of ascorbic acid run the entire gamut of medical knowledge. Body needs are so great that so called minimal daily requirements must be ignored. A genetic error is the probable cause for our inability to manufacture ascorbic acid, thus requiring exogenous sources of vitamin C. Simple dye or chemical test are available for checking individual needs. Ascorbic acid destroys virus bodies by taking up the protein coat so that new units cannot be made, by contributing to the break-down of virus nucleic acid with the result of controlled purine metabolism. Its action in dealing with virus pneumonia and virus encephalitis has been outlined. The clinical use of vitamin C in pneumonia has a very sound foundation. In experimental tests monkeys kept on a vitamin C free diet all died of pneumonia while those with adequate diets remained healthy.⁶² Many investigators have shown an increased need for ascorbic acid in this condition.^{63,64} Brody in 1953 after studying vitamin C and colds in college students advised that ascorbic acid be given early and often in sufficient amounts. Regnier⁶⁵ reporting in review of Allergy found that the larger the dose of ascorbic acid the better were the results. Our findings resulted in a schedule of one gram each hour for 48 hours and then 10 grams each day by mouth. Those under ten at least one gram for each year of life.

Virus Encephalitis

Virus encephalitis is a deadly syndrome and must be treated heroically with intravenous and/or intramuscular injections of ascorbic acid. We recommend a dose schedule of from 350 mg to 700 mg per Kg. body weight diluted to at least 18 c.c. of 5D water to each gram of "C". In small children, 2 and 3 grams can be given intramuscularly, every 2 hours. An ice cap to the buttock will prevent soreness and induration. Ascorbic acid in amounts under 400 mg per Kg. body weight can be administered intravenously with a syringe in dilutions of 5 c.c. to each one gram provided the ampoule is buffered with sodium bicarbonate with sodium Bisulfite added. As much as 12 grams can be given in this manner with a 50 c.c. syringe. Larger amounts must be diluted with "bottle" dextrose or "saline" solutions and run in by needle drip. This is true because amounts like 20 to 25 grams which can be given with a 100 c.c. syringe can suddenly dehydrate the cerebral cortex so as to produce convulsive movements of the legs. This represents a peculiar syndrome, symptomatic epilepsy, in which the patient is mentally clear and experiences no discomfort except that the lower extremities are in mild convulsion. This epileptiform type seizure will continue for 20 plus minutes and then abruptly stop. Mild pressure on the knees will stop the seizure so long as pressure is maintained. If still within the time limit of the seizure the spasm will re-appear by simply withdrawing the hand pressure. I have seen this in two patients receiving 26 grams intravenously with a 100 c.c. syringe on the second injection. One patient had poliomyelitis, the other malignant measles. Both were adults. I have duplicated this on myself to prove no after effects. Intramuscular injections are always 500 mg to 1 c.c. solution. With continuous intravenous injections of large amounts of ascorbic acid, at least one gram of calcium

gluconate must be added to the fluids each day. This is done because we have found that massive doses of ascorbic acid pulls free calcium ions from the vicinity of the platelets or from the calcium-prothrombin complex as the lactone ring of dehydroascorbic acid is opened. The first sign of calcium ion loss is "nose bleeding". This differs from the nosebleed found, at times, in cases of chicken pox or measles. Here it represents frank scurvy from vitamin C deficiency. The pathology being "Capillary fragility".⁶⁶

Burns

A new treatment for burns has been outlined, which if followed will eliminate skin grafting and plastic surgery. It is probably too simple to gain early acceptance. The literature has been suggesting the value of ascorbic acid in burns for many years. Proper local application and the amount for systemic usage has been misleading. One only need see one case properly treated with ascorbic acid to appreciate its importance. If ascorbic acid can destroy the exotoxin of tetanus, as Jungeblut demonstrated, it can also destroy the exotoxin of *Pseudomonas*. Ascorbic acid plays an important role in maintaining fluid balance in the body. Ruskin pointed out that the vitamin activates an enzyme arginase, which breaks down the amino acid arginine, resulting in production of urea which is one key to tissue fluid balance.

Pregnancy

The simple stress of pregnancy demands supplemental vitamin C. This amount will vary with the individual. The silver nitrate-urine test will simplify these findings. Vitamin C seems especially concerned with mesenchymal tissue. When one considers the demands of the fetus and infant, especially premature babies, it is obvious that high vitamin C intakes are required during pregnancy because this "parasite" will drain available "C" from the mother. Greenblatt⁶⁷ reports excellent results following the oral administration of vitamin C in the therapy of habitual abortion. In my own practice I was able to take women who had had as many as five abortions without a successful pregnancy and carry them through two and three uneventful pregnancies with the use of supplemental vitamin C. The German literature is "stacked" with articles recommending high doses of vitamin C during gestation because they believe that this substance is of great benefit in influencing the health of the mother and in preventing infections. The vital contribution of ascorbic acid to the body tissues can be summed up in the formation and maintenance of normal intercellular material, especially in the connective tissue, bones, teeth, and blood vessels. Genetic errors might be prevented if prospective mothers were advised to take 10 or more grams of ascorbic acid daily. It is significant that we found in the simple stress of pregnancy, a normal physiological process, that equivalent requirements paralleled those found in the rat when under stress. Experiments by King et al.⁶⁸ have shown that the need for supplemental vitamin C begins with the embryo.

Kidney Stones

The "scare" factor of large doses of ascorbic vs. kidney stones has been laid to rest. Since the urine is usually pH-6, one can see that the opening of the lactone ring is a slow process. This reaction takes place in tissues and is probably regulated by the

amount of glutathione present. The important considerations are that one must have a concentrated urine, that stasis must be a factor and that the urine must be alkaline for any appreciable amounts of the crystalloids to precipitate out. This will never occur with massive ascorbic acid therapy. Furthermore, it has been shown that the controls in a given experiment had almost as much oxalic acid spill as did those volunteers taking 9 grams of ascorbic acid daily.

Insect - Snake Bites

The quickness of results in snake bite, spider bite, hornet stings and caterpillar reactions demonstrates the usefulness in saving lives. It is best to give the vitamin intravenously with a syringe since bottle preparations are too time consuming. One precaution must be given. There exist a 2 gram ascorbic acid ampule, and ironically it is the only one to my knowledge approved by the Food and Drug Administration, which might "kill" if used undiluted in a syringe. This lethal factor is due to the preservatives added. Each ampule contains 2 grams sodium ascorbate. Vehicle contains: Monothio-glycerol 0.14%; Sodium Formaldehyde Sulfoxylate 0.05%; Methyl Paraben 0.13%; Propyl Paraben 0.015%. Neutralized to pH 6 with Sodium Bicarbonate; Water for injection q.s. This ampule can be used intravenously ONLY when diluted to at least 25 c.c. to one gram. One sometimes will be confronted with extraordinary allergic and shock symptoms along with acute respiratory obstruction. In these situation one must employ Benadryl intravenously and/or intramuscularly and an adrenocortical hormone such as Decadron. These can be given by a nurse while the ascorbic acid is being prepared. In their absence a second "syringe" dose of ascorbic acid will suffice. Fluids by mouth should be given to prevent or correct thirst which all patients seem to experience.

Diabetes

Large doses of ascorbic acid do not cause diabetes mellitus in humans as has been suggested. On the contrary 10 grams daily, by mouth, has proved to be beneficial. The fact that 10 grams will allow them to heal wounds like normal individuals will save many legs in the future. Lamden, a bio-chemist, instigated these fears by misinterpretation of the results reported by Patterson using the Ketone formula intravenously in rats.

In Surgery

In surgery the use of ascorbic acid resolves itself into a "must" situation. The 24 hour frank scurvy levels should be sufficient evidence to encourage all surgeons to use vitamin C freely in their fluids. Proper employment of vitamin C by the surgeons will all but eliminate the post-surgery deaths.

In Malignancy

The part very large doses of ascorbic acid given intravenously over a prolonged period offers a medical challenge. From cabbage and tomatoes grown in the carbon-14 chambers radioactive ascorbic acid can be extracted, which can be used in tracer studies. At least one re-search team has demonstrated that in cancer all available "C" is mobilized at the site of the malignancy. Lauber and Rosenfeld reported that "C" is mobilized from the tissues of the body and selectively concentrated in traumatized areas. In one hopeless

case we administered 17 grams daily for 92 consecutive days without changing the blood or urine levels from that associated with scurvy. This is the reason we believe a dose range of 100 grams to 300 grams daily by continuous intravenous drip for a period of several months might prove surprisingly profitable. Blood chemistry should be followed daily with such an investigation. Schlegel found that even a dose of 1.5 grams a day, by mouth, would prevent bladder cancer.

Barbiturate Poisoning

Our findings in no less than 15 cases of barbiturate poisoning suggested that no death should occur from this error in judgment. We also observed the dramatic effect of 12 grams intravenously on blood pressure associated with shock. The shock seen in heat stroke had been corrected by the time the injection was completed. The dose range used was 500 mg per Kg body weight.

Tetanus - Trichinosis

The use of ascorbic acid with Tolserol in the treatment of Tetanus should be accepted as universal treatment. Here again the dose must be proper. Our case as reported will serve as a guide in making these calculations. Ascorbic acid along with Para-Aminobenzoic acid is curative in Trichinosis. Both drugs are administered by mouth. It is estimated that at least 5 million cases of chronic Trichinosis exists in the United States. Just nine days of treatment would return these individuals to normal. In our cases 10 grams ascorbic acid was given daily and Para-Aminobenzoic acid was employed in high range. Four to six grams to start then three grams every 2 hours for eight times. For the remainder of the nine day schedule it was given 3 grams every two hours during the day and every three hours during the night.

Viral Hepatitis

Ascorbic acid is the drug of choice in viral hepatitis. The dose used ranges from 400 mg to 600 mg per Kg body weight, depending on the severity of the disease. It should be given every 8 to 12 hours. Ten grams ascorbic acid daily in divided doses is also given by mouth. Those under 10 years the usual schedule of at least one gram for each year of life.

Multiple Uses

We have reviewed many other pathological conditions in which ascorbic acid plays an important part in recovery. To these might be added Cardiovascular Diseases, Hypermenorrhea, Peptic and Duodenal Ulcers, Post-operative and Radiation Sickness, Rheumatic Fever, Scarlet Fever, Poliomyelitis, Acute and Chronic Pancreatitis, Tularemia, Whooping Cough and Tuberculosis. In one case of scarlet fever in which Penicillin and the Sulfa drugs were showing no improvement, fifty grams ascorbic acid given intravenously resulted in a dramatic drop in the fever curve to normal. Here the action of ascorbic acid was not only direct but also as a synergist. A similar situation was observed in a case of lobar pneumonia. In another case of purperal sepsis following a criminal abortion the initial dose of ascorbic acid was 1200 mg per Kg body weight and two subsequent injections were at the 600 mg level. Along with Penicillin and Sulfadia-

zine an admission temperature of 105.4°F was normal in nine hours. The patient made an uneventful recovery. In one spectacular case of Black Widow⁶⁹ spider bite in a 3½ year old child, in coma, one gram calcium gluconate and 4 grams of ascorbic acid was administered intravenously when first seen in the office. Four grams ascorbic acid was then given every six hours using a 20 c.c. syringe. She was awake and well in 24 hours. Physical examination showed a comatosed child with a rigid abdomen. The area about the umbilicus was red and indurated, suggesting a strangulated hernia. With a 4 power lense, fang marks were in evidence. Thirty hours after starting the vitamin C therapy the child expelled a large amount of dark clotted blood. There was no other residual. A review of the literature confirmed that this individual has been the only one to survive with such findings; the others were reported at autopsy. Ten grams vitamin C and 200 mg to 400 mg vitamin B-6, by mouth, daily will "shield" one from mosquito bites. Twenty percent will also require 100 mg vitamin B-6 intramuscularly each week.

General Nutrition

Vitamin C plays a very important role in general nutrition. Deficiency of this substance in sufficient amounts can be a factor in loss of appetite, loss of weight or failure to grow, muscular weakness, anemia and various skin lesions. The relationship between vitamin C and the health of the gums and teeth has long been recognized. Laboratory studies on gum-teeth connective tissue have reaffirmed this relationship.⁷⁰ Our son who will be 19 in July has never developed a tooth cavity. Since age 10 he has received at least 10 grams ascorbic acid, daily, by mouth. Before age 10 the amount given was on a sliding scale.

Intra-Venous Application

Ascorbic acid must be given by needle to bring about quick reversal of various "in-sults" to the human body. We have found that doses must range from 350 mg to 1200 mg per Kg body weight. Under 400 mg per Kg of body weight the injection can be made with a syringe provided the vitamin is buffered with sodium bicarbonate with Sodium Bisulfite added. Above 400 mg doses per Kg body weight, and a particular ampoule described in this summary, the vitamin must be diluted to at least 18 c.c. of 5 per cent dextrose in water, saline in water or Ringer's solution. Many times Adenosine 5-Monophosphate, 25 mg in children and 50 to 100 mg in adults, given intramuscularly, is necessary to achieve results. The aqueous solution is more effective for quick results, although Adenosine in Gel can be employed. In debilitated individuals or when the pathology is serious, Desoxycorticosterone Acetate (DCA), aquoua solution, must also be added to the schedule. Usually 2.5 mg for children and 5 mg for adults is the daily intramuscular dose required. Sudden swelling of the feet indicates abnormal sensitivity and the drug must be discontinued.

It must be remembered when using ascorbic acid that experiments on man are the only experiments which can give positive evidence of therapeutic action in man. Likewise, the use of ascorbic acid in human pathology must follow the Law of Mass Action: "In reversible reactions, the extent of chemical change is proportional to the active masses of the interacting substance."

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APPENDIX

Case History: Pesticide Poisoning—Three boys ranging in years from age seven to age 12 were walking along a North Carolina Highway. They were caught in the “spray” of a dusting airplane. The youngest boy had been covered by the other two and so received little exposure. He was seen in the emergency room of the local hospital and sent home. The other two boys had different physicians. One lad age 12, under our care, was given 10 grams of ascorbic acid with a 50 c.c. syringe every 8 hours. The concentration was one gram for each 5 c.c. diluent. He was returned home on the second hospital day. The third boy received supportive treatment but did not receive ascorbic acid. His body was something to see. The spray had produced an allergic dermatitis as well as a chemical burn. He died on the 5th hospital day.

Case History: Nasal Diphtheria—Three children, living in the same neighborhood, developed nasal diphtheria. All three children had different physicians. A little girl under our care was given 10 grams ascorbic acid, intravenously, with a 50 c.c. syringe every 8 hours for the first 24 hours and then every 12 hours for two times. She was then put on one gram ascorbic acid every two hours by mouth. She lived and is now a graduate nurse. The other children did not receive ascorbic acid and both died. Our young patient also received 40,000 units diphtheria antitoxin which was given intraperitoneal. The other children also were administered the antitoxin.

Case History: Poliomyelitis—Although we were able to cure many cases of polio with massive doses of ascorbic acid, one single instance demonstrates the value of vitamin C. Two brothers were sick with poliomyelitis. These two boys were given 10 and 12 grams of ascorbic acid, according to weight, intravenously with a 50 c.c. syringe, every eight hours for 4 times and then every 12 hours for 4 times. They also were given one gram

every two hours by mouth around the clock. They made complete recovery and both were athletic stars in high school and college. A third child, a neighbor, under the care of another physician received no ascorbic acid. This child also lived. The young lady is still wearing braces.

Case History: Acute Virus Infection representing Deadly Virus Syndrome.—Cases with paralysis are extremely interesting in as much as they challenge diagnostic prowess. One of our cases, a female age 58, demonstrated three different types. She entered the hospital because of a convulsive seizure. She had had a lingering cold for ten days. She experienced three additional convulsive seizures after hospital admission. The temperature was 100.8°F, pulse 140, respirations 32. She was extremely restless. Twenty-four grams ascorbic acid in 360 c.c. 5D water was given intravenously for three times at 8 hour intervals. One gram calcium gluconate was added to the first and third bottle. Twenty four hours following admission and 72 grams ascorbic acid in the blood stream, patient was awake and rational but completely paralyzed, right arm and leg. Five grams ascorbic acid was given in fruit juice every 6 hours by mouth and 6 grams ascorbic acid along with a B complex preparation was given intravenously, daily for eight additional days. The right arm and leg returned to normal 48 hours after admission. Classical pellagra was also corrected during this hospital stay.

Case History: Repeating virus infection—This case proved that adequate ascorbic acid therapy must be continued long enough to destroy all virus bodies, otherwise the infection will recur. In 1960, I treated a seven year old boy, off and on, over a period of six weeks, for influenza like symptoms. Therapy included one of the mold derived drugs, sulfadiazine and 5 to 10 grams ascorbic acid by mouth. On three different occasions this treatment schedule was dramatically effective. When the child became ill for the fourth time, the administration of the above antibiotics and oral vitamin C had no reversing effect. On the third day of this illness the child suddenly became lethargic and just as suddenly to frank stupor. The temperature which had been running low grade was now 102.6°F. At this point all oral medication was discontinued. I immediately gave six grams of ascorbic acid intravenously with a 30 c.c. syringe. He was awake and asking, “what happened” in 5 minutes. Six grams ascorbic acid was given in 4 hours and then at 6 hour intervals for two additional doses. The recovery was complete in 24 hours and remained so. Ascorbic acid was again started by mouth giving 5 grams in juice every 8 hours. After one week, this was reduced to the usual daily “take” of seven grams. I had ample opportunity to observe this case—the child was our son.

Case History: Snake bite—Child of 4 years was struck on the lower leg by a large highland moccasin at 7:00 P.M., while at play in the yard of her country home. Seen in the emergency room of the local hospital at 7:30 P.M., the child was vomiting, was crying because of severe pain in her leg, which she held with both hands above the “fang marks”. Fever was 99.0°F. Four grams of ascorbic acid was given intravenously at 7:35 P.M. with a 20 c.c. syringe. The following 25 minutes were taken to follow a skin test on anti-venom. At this time and before the anti-venom was administered the child had

stopped vomiting, she had stopped crying and was sitting on the emergency room table, laughing and drinking a glass of orange juice. She commented: "Come on, Daddy, I'm all right now, lets go home." She was allowed to return home with the understanding that her father would give me a report, by phone, each hour during the night. This he did. His report, each time, was that the child was sleeping as usual and that except for moderate swelling to the "calf of the leg", appeared normal. Seen in the office at 10:00 A.M. the following morning she still demonstrated the small amount of swelling of her leg and had $\frac{1}{2}$ degree fever. She was given a second dose of 4 grams of ascorbic acid intravenously. Seen at 5 P.M. she had no fever but the swelling remained constant. There was no pain. The following day, 38 hours after being bitten, she was completely normal. Since this was our first case of snake bite treated with vitamin C, we elected to give an additional 4 grams of ascorbic acid on this visit. No other antibiotics were given and none was required. Since she had had a booster injection of tetanus toxoid in recent months, none was given at this time. Comparing this to an earlier case of snake bite in a 16 year old girl, struck by a moccasin of about the same size, as gauged from the fang marks, on the hand while pulling tobacco plants, and who was hospitalized for three weeks. She was given 3 doses of anti-venom. The arm was compressed continuously with magnesium sulfate solution. Swelling was four times that of the opposite arm and striae developed over the entire surface. This patient received no vitamin C other than that found in a regular hospital diet. Morphine was required to control pain. (We no longer use anti-venom.)

Case History: An Insidious virus—This was a child of 18 months. She was seen in the driveway to my home at about 7:00 P.M. The history was brief. The child had strangled on food while eating supper. A cursory examination given in the front seat of an automobile revealed an extremely restless, whining child. The temperature was 98.6°F (axillary 10 minutes-corrected). There was no obstruction to the air-ways. We did elicit the information that the child had had a cold for several days. We also learned that the child's mother had taken her for a long stroller ride the previous day—which in this area was damp and cold. Frankly the impulse to send the child home was great.

Remembering that I had seen children dead within 30 minutes to two hours after hospital admission without treatment, I decided to buy some time. The Uncle was asked to take the child to the emergency room of the local hospital. The nurse on duty was given an order to take a rectal temperature and then give a fleets enema. If the results proved un-satisfactory, she was to repeat the procedure in 30 minutes using a normal saline solution. Approximately 45 minutes after leaving my home, the intern on duty reported by phone, that the child was unconscious to a point where she responded only to pain stimuli. The enema had not been given. Going at once to the hospital, conditions were found as described. The little patient was lying motionless on the examining table. Using a suitable size rectal tube I gave the enema with good results. The stool was normal. Rectal temperature taken at the hospital was 98.4°F (corrected). The pulse rate was 152 per minute and respirations were 32 per minute. It was impossible to visualize the throat because the mouth was "locked" as one finds after stimulation in lockjaw. Our impression was that the virus had now entered the brain. Thirty grams of ascorbic

acid, in divided doses, was given intramuscularly over a period of 36 hours. Crystalline penicillin was started on the second day and 300,000 units were administered in divided doses over the next three days. This was added to block secondary invaders. One hour following admission we applied a 4 x 4 gauze, saturated with tap water, to the child's lips. The sucking reflex was still intact, but the child immediately strangled. Turning the child head down, the small amount of water ran from its nostrils. Now it was clear. It was this "bulbar phenomenon" that was at play when the child was eating supper. The nursing log showed the temperature to be 99.0°F (corrected) 1½ hours after admission and 1½ hours later it was recorded at 100.0°F (corrected). The nursing log at this time read: "Shows no sign of consciousness." Temperature was 101.2°F four hours after admission and was 102.4°F (corrected) after six hours. Now the nursing log read: "Baby swallowed water without difficulty." At this point the temperature curve started back down and by 7:00 A.M. (11 hours following admission) the child was alert and taking water freely from a spoon. Twenty eight hours after the first injection of ascorbic acid the temperature was normal. Water, milk and orange juice were now taken from a bottle. Cecon (liquid vitamin C) was given by mouth. Discharge was on the 5th hospital day. The initial low fever recording indicated that the child was dying; after ascorbic acid therapy she began to respond, thus the fever. After the virus was killed, the temperature returned to normal.

Case History: Monoxide Poisoning—State highway employee carried into my office in unconscious condition. He was a known diabetic. The breathing was not Kussmaul type and his skin was warm and dry. We elicited the information that he had been found in the cab of his truck with the windows closed and the engine running. It was a cold Winter day. Entertaining a diagnosis of Monoxide intoxication we immediately gave 12 grams ascorbic acid with a 50 c.c. syringe using a 20 gauge needle. (We employ a 20 G needle when using a 50 c.c. syringe; 21 G needle for a 30 c.c. syringe; 22 G needle for a 20 c.c. syringe and a 23 G needle for a 10 c.c. syringe. This assists in controlling the rate of flow which is important, especially, in young children). Within 10 minutes the patient was awake, sitting up on the edge of the examining table, rubbing his eyes and saying: "Doc, what in the world am I doing up here in your office." He returned to his place of employment within 45 minutes.

Case History #1: Acute Virus Pancarditis—A five year old boy was admitted to the local hospital with history of having a "re-lapse" after recovery from measles. The physical findings showed a thready and feeble pulse. A distinct rub was in evidence by auscultation. The EKG showed RS-T deviations. The temperature was 105°F. Ascorbic acid calculated at 400 mg per Kg body weight was given intravenously with a syringe. Within two hours the picture had almost reverted to normal. Injection of Vitamin C was repeated in 6 hours and again at 12 hours. A fourth injection was given after 24 hours although the patient was clinically well. The child returned home on the 4th hospital day.

Case History #2: Acute Virus Pancarditis following a deep cold.—The findings approximated those of case #1. The parents elected to take the child to Duke Medical

Center. Six grams of ascorbic acid was given by needle before starting the trip to the hospital which was 60 miles away. Upon arrival at the Medical Center the child had made such dramatic response to the single injection of ascorbic acid that the parents were tempted to return home. The receiving physician questioned the sickness of the child as being out of proportion to that relayed by me during our telephone conversation. The parents assured the physician that the child had been seriously ill, but that the change came about after receiving the ascorbic acid. Although 50 grams (25 ampoules) of ascorbic acid was sent along with the parents, none was given because the physician in charge stated that he would be afraid to give that size dose, intravenously, to a child. The fact that we had administered six grams, which represented a dose of 400 mg per Kg body weight, apparently had no influence. Laboratory findings, however, confirmed our impression and the child was hospitalized for two weeks. Two additional injections of vitamin C would have cured the child in 24 hours.

Case History: Acute Pancreatitis—Adult Male seen in the emergency room of local hospital complaining of severe, agonizing pain in the epigastrium which radiated to the back. Nausea and vomiting were present. Serum amylase studies showed a concentration of 345. This was the 4th such attack experienced by this patient. Sixty grams ascorbic acid in 700 c.c. Dextrose in water was given intravenously. 20 mg Pantapone was given in the emergency room. No additional opiates were required. The patient made an uneventful recovery. He was placed on 10 grams ascorbic acid by mouth and has not had a recurrence in almost 5 years. He has, however, developed mild diabetes mellitus which is now controlled with diet and vitamin C.

END

I am in full agreement with Lancelot Hogben who said: "A scientific idea must live dangerously or die of inanition. Science thrives on daring generalizations. There is nothing particularly scientific about excessive caution. Cautious explorers do not cross the Atlantic of truth."

FREDERICK R. KLENNER, M.D., F.C.C.P. REIDSVILLE, NORTH CAROLINA

A native of Pennsylvania, Dr. Klenner attended St. Vincent and St. Francis College, where he received his B.S. and M.S. degrees in biology. He graduated magna cum laude and was awarded a teaching fellowship there. He was also awarded the college medal for scholastic philosophy. There followed another teaching fellowship in chemistry at Catholic University, where he pursued studies for a doctorate in physiology.

Dr. Klenner then 'migrated' to North Carolina and Duke University to continue his studies. He arrived in time to use his knowledge in physiology and chemistry to free the nervous system of the frog for a symposium by immersing the animal in 10% nitric acid. Taken in tow by Dr. Pearse, chairman of the department, he was finally persuaded to enter the school of medicine. He completed his studies at Duke University and received his medical degree in 1936.

Dr. Klenner served three years in post graduate hospital training before embarking on a private practice in medicine. Although specializing in diseases of the chest, he continued to do general practice because of the opportunities it afforded for observations in medicine. His patients were as enthusiastic as he in playing guinea pigs to study the action of ascorbic acid. The first massive doses of ascorbic acid he gave to himself. Each time something new appeared on the horizon he took the same amount of ascorbic acid to study its effects so as to come up with the answers.

*Dr. Klenner's list of honors and professional society affiliations is tremendous. He is listed in a flock of various "Who's Who" registers. He has published many scientific papers throughout his scientific career.

Dr. Fred Klenner describes the use of injectable vitamin C as part of the treatment for lockjaw (tetanus) in a six-year-old boy. He also describes using injectable vitamin C to successfully treat a four-year-old child bitten by a mature highland moccasin. (Note also, he instructed the father of the snake-bitten child to call him every hour throughout the night to report on the child's condition following his first use of this treatment.)—*R.D.M.*

Recent Discoveries in the Treatment of Lockjaw with Vitamin C and Tolserol

Dr. Fred R. Klenner, Reidsville, N.C.
Tri-State Medical Journal, July 1954, Vol. 2, No. 2, pp. 7-11
Second in a Series of Two

The purpose of this paper is to dispel the popular belief that tetanus is a difficult disease to cure. It is bold, but correct to say that the number of cases terminating fatally from the disease are equaled by those who die from the treatment. Evidence will be presented to show that the antitoxin has no curative value and at the best is harmful. Convulsive seizures must be controlled, but it is wrong to employ a drug for this purpose that tends to deprive the patient of his sensorium. Many patients have been lost, not only with tetanus but also from the many other disease conditions, simply because the treating physician blindly followed a recommendation set down by a colleague who by "Fate" was in a position of authority. Too few of those who write appreciate the responsibility of their words. Unfortunately, in medicine, the driver's seat is still at the back. It is rare, indeed, to find any two authorities offering the identical treatment for any given disease. Some much used volumes give five, ten, or even fifteen different remedies for a given disease; this can only lead to "coin tossing." Yet MAN in his search for health still comes to the doctor. This condition will prevail until we assume enough courage to have but ONE textbook for the practice of medicine; this should be loose-leaf.

Case History: White boy of 6 years. Did not receive the required pre-school injections. Severe asthmatic since infancy. Reported to have had diphtheria March 1951; no smears or culture made. Present illness thought to have started three weeks before admission with severe attack of asthma which lasted for two weeks. This episode was associated with abdominal cramps, unexplained at the time, and a generalized sensation of muscle tightness. Six days before admission he developed drooping of the eyelids. He also found it difficult to smile (perpetual with this boy under normal circumstances) and there was definite resistance whenever he attempted to fully open his mouth, like in a yawn. Abdominal cramps were now more pronounced and they were experienced more frequently. Two days prior to admission his abdominal muscles assumed boardlike

rigidity which was synchronized with the abdominal pain and these episodes were being experienced more often while increasing in duration. His diet was self limited to liquids due to the inability to open his mouth more than 30%; this created pain at the temporomaxillary joint and was always followed by the sudden "involuntary" clamping of his jaws. On the day of admission he had progressed to a stage when the slightest stimulation would contract his back muscles with such force that he would form an arch with his body resting on his feet and head. Sweating was profuse during this time; respirations were absent. When the clonic spasm was released he would lie limp and exhausted.

The physical examination added little to this picture. The temperature was 100.4° F., respirations shallow 20 to 25 per minute, the pulse was rapid but not thready, running between 120 and 130. He could "push" his tongue to the margin of his lips and a facial expression was impossible. A few "terminal rales" could be heard in both lung fields. The right patellar reflex was exaggerated and since this elicited a convulsive seizure the other reflexes were not attempted. His course in the hospital was interesting but not dramatic. The most trying period was spent in combating the pathology resulting from allergy. There was a history of a fall in the pony yard resulting in "brush burns" of his hands about one week before the onset of the "peculiar asthma attack." (It must be added that many a devout person offered sincere prayer for this lad's recovery. I humbly submit that Providence in hearing these supplications, did employ my intellect in carrying out His design.)

In the past it was thought that successful therapy depended upon four factors: (1) Early and adequate use of antitoxin; (2) Sedation to the point of narcosis; (3) Wound debridement; (4) Competent, intelligent, continuous nursing; (5) Five percent hydrogen peroxide to which Tr. of iodine has been added for cleansing the wound, magnesium sulfate given intravenously as a 20% solution in the amount of 50 cc, curare, frequent warm baths, spinal tap with replacement of fluid with anti-tetanus serum and a quiet, dark room.

Today the treatment of tetanus has resolved itself into a plan best suited to combat the convulsive seizures. Except for one single dose of antitoxin (75,000 units) given deep intramuscularly above the portal of entry if this is known or is possible, the use of this "agent" should be forgotten. Its employment, presently, is intended more for the legal protection of the attending physician rather than for the betterment of the patient. Our case will prove that it has no value and in all probability was harmful. Teale and Embleton reported that the toxin does not pass from the capillaries to the tissue of the central nervous system, nor from the choroid plexus to the cerebrospinal fluid, and that it is blocked from reaching the cord along the afferent nerves by the posterior root ganglia. By inference they concurred with Meyer and Ransom in believing that the path taken by the poison was the motor nerves. MacCallum pointed out that the antitoxin cannot travel from the circulation into the nervous system and that unless it be injected into the nervous tissue, it is relatively valueless. Meyer and Ransom showed that the injection of antitoxin into the nerve ABOVE the point of inoculation would BLOCK and neutralize the toxin. Davison advocates the use of tetanus toxoid 0.1 cc given intradermally for five consecutive days as a means of boosting the patient's antitoxin titer.

The most important therapeutic measures available are massive doses of vitamin C and Tolserol, both given intravenously. Jungeblut reported that vitamin C, when added to tetanus toxin "in vitro," brings about inactivation of the toxin. He felt, however, that the mechanism of the inactivation of tetanus toxin by vitamin C was fundamentally different from that of toxin-antitoxin reactions. In one experiment he observed that guinea pigs injected with a mixture containing critical amounts of toxin and vitamin C died with tetanus if the mixture was not incubated and LIVED if the mixture was previously incubated. (We believe the human body to be a first class incubator.) This work of Jungeblut followed, in a fashion, the findings of Imamura who, in 1929, reported inactivation of tetanus toxin by adding it to ovarian follicular fluid. Corpus luteum is now known to contain a high concentration of vitamin C. We have found massive doses of vitamin C to be dramatically effective in hundreds of cases in which the offending poison was an exotoxin or a virus. (Here I must inject the story of a four-year-old child bitten on the leg by a mature, highland mocassin. This case is related to tetanus in that both conditions offer the "exotoxin" as the killing agent. The child was bitten at 7 p.m. while playing in the yard. Seen in the emergency room of the local hospital at 7:30 p.m., she was vomiting, was crying because of severe pain in her leg which she held above the "fang marks" and had a 99.2° F. fever. Four grams of vitamin C was given intravenously at 7:35 p.m. The following 35 minutes was taken up preparing and skin testing anti-venom serum which was given at 8:00 p.m. At this time and before the anti-venom was administered she had stopped vomiting, had stopped crying and was sitting on the emergency room table laughing while she drank an orangeade. Her comment was: "Come on, daddy, I'm all right now." She was not admitted to the hospital but was allowed to return home with the understanding that the father would give me a report, by telephone, each hour throughout the night. This he did. His report each time was that she was sleeping as she usually did, and that other than a small amount of swelling up to the calf of her leg, appeared normal. She was seen in my office the following morning at 10 a.m. At this time she had ½ degree of fever and about the same amount of swelling described by her father during the night reports. She had had a "big" breakfast and wanted to know if she could play when she returned home. She was given 4 grams of vitamin C intravenously and sent home. Seen the same day at 5:00 p.m. she had no fever and about the same amount of swelling. She was given 4 grams of vitamin C intravenously. The following morning, 38 hours after being bitten, she was completely normal. As a precautionary measure 4 grams of vitamin C was given intravenously. This was the end of the snake bite, except that she carried the fang marks for a considerable time. No other antibiotic was given for secondary wound invaders as a result of the bite and none was required. This treatment was first worked out by me in dogs and published in hunting and fishing magazines. Several physicians have cured rattlesnake bites using this treatment schedule; their voluntary letters are in my files.) The vitamin must be given by needle in massive doses and around the clock to obtain these results.

Intravenous TOLSEROL, given in adequate amounts, has no equal in controlling the convulsive seizures found in tetanus. In our case of the six-year-old boy weighing 20 Kg. we gave as an initial dose 200 mg of Tolserol in 500 cc of D5 water at a rate of 35 drops

per minute. Since no dose schedule was available for children at that time (September 1951), we experimented with this amount since we did not desire too great a relaxation. Prostigmin was made available for this emergency. There was no response to this amount of Tolserol, so after six hours an additional 800 mgm was given, using the same type of diluent. The results obtained proved that this was the drug of choice in producing relaxation and preventing convulsive seizures in tetanus. This fact was apparent before the fluid run was completed. Subsequent doses of Tolserol were set at 1000 mgm. This amount gave complete control of all muscle spasm for a period of 60 hours. Under the influence of intravenous Tolserol the patient immediately began to take nourishment by mouth, was not disturbed by noises in excess of what should be expected in a hospital and did not require a darkened room. Nursing care was limited to that given by "floor nurses," although we did keep a companion in the room at all times as a psychological measure. The same day that intravenous Tolserol was given the patient played with toys in his bed and used crayons to color pictures in a color book. After about 60 hours this interest was suddenly lost and mild spasms returned. This pattern was just as suddenly reversed by giving another 1000 mgm of Tolserol intravenously. Other types of therapy were employed in this case. A review of his hospital course will argue the case for vitamin C and intravenous Tolserol. At only one period of his hospitalization was the outcome in doubt and this was due to a reaction to serum. Here again Tolserol and vitamin C saved the day.

He was admitted 9/1/51 at 30 minutes past noon. Two grams vitamin C were given intravenously at 1:00 p.m. Liquids taken freely throughout afternoon. 6:00 p.m. 2 grams of vitamin C. (All vitamin C and Tolserol given in this case was administered intravenously.) At 8:15 p.m. child reported crying loudly. A.S.A. grains V given by mouth with some difficulty. 9:00 p.m. 2 grams of vitamin C. At 10:40 p.m. an S.S. enema was given with good results. The procedure did not excite muscle spasm. 12:00 midnight 4 grams of vitamin C and one 10 cc ampule calcium gluconate. Child sleeping. At 3:00 a.m. 4 grams vitamin C. Patient having moderate abdominal cramps; no difficulty in swallowing. 6:00 a.m. condition same; given 4 grams vitamin C. 8:00 a.m. some difficulty in swallowing; 4 grams vitamin C given at 9:00 a.m. and by 10:00 a.m. was resting quietly. Sleeping at 11:00 a.m. and at 12:00 noon voided 100 cc urine. (From this point kidney output was normal.) Taking fluids freely by mouth. At 1:00 p.m. 4 grams vitamin C and 600,000 units procaine penicillin. The entire afternoon was spent "lying quietly" in bed. Fluids now protinal in milk and egg in milk; no difficulty in swallowing. At 6:00 p.m. and 9:00 p.m. 4 grams of vitamin C. Nembutal suppository grains 2 ordered by intern but there was no restlessness. The explanation for this order was "so the boy would get off early to sleep." At 12:00 midnight was given aspirin grains V, 4 grams of vitamin C and 600,000 units procaine penicillin. The rationale of the penicillin was to prevent secondary pulmonary pathology. The night of September 3rd was uneventful; he received 4 grams of vitamin C at 3:00 a.m. and at 6:00 a.m. Had mild abdominal cramps, off and on, through the morning. At 10:00 a.m. 4 grams of vitamin C; sleeping at intervals. Because of "outside pressure" 25,000 units TAT were given with saline intravenously, after skin testing for sensitivity. This was at 12 noon. By 1:00 p.m. his temperature was up to 101° F. rectally, the highest since admission; refused egg in milk. 2:00 p.m. voided 300 cc urine. At 3:00

p.m. he was crying because of severe pain in his abdomen. Floor nurse reported in her daily log—"an uncomfortable period since antitoxin." 4:00 p.m. 4 grams vitamin C, refused all liquids but by 5:00 p.m. was sleeping. Since antitoxin therapy was not our decision we elected to be heroic and give it a test to prove its lack of value.

(I will never forget a case of "lockjaw" in an adult white female that was my duty to treat as a house physician at Moore County General Hospital in 1937. Notes which I made at that time show that this patient died from asphyxia less than one hour after receiving 30,000 units of tetanus antitoxin intravenously. The serum was not diluted in saline as we employed in this case but it was given very slowly. Intravenous sodium amytal failed to release the convulsive seizure in this woman.)

At 8:00 p.m. 50,000 units T.A.T. in saline given intravenously; 4 grams of vitamin C given after completion of antitoxin. 9:00 p.m. he was, as before when T.A.T. was given, crying because of severe abdominal pain; his back was rigid and bowed. This picture continued fairly constant until 12:00 midnight; 4 grams vitamin C and 600,000 units penicillin given. By 1:00 a.m. he was resting comfortably and by 2:00 a.m. the nurse recorded—"abdomen more relaxed, still has slight attacks of pain but much further apart." 4:00 a.m. 4 grams vitamin C and he slept until bath at 7:00 a.m. At 8:00 a.m. 50,000 units T.A.T. intravenously in saline: aspirin grains V. 9:00 a.m. was having frequent sharp abdominal pain; nourishment by mouth was a bottle of carbonated drink and $\frac{1}{2}$ glass of milk. 12:00 noon 4 grams vitamin C and 4 grams again at 4:00 p.m. Comfortable throughout afternoon. At 7:30 p.m. 20,000 units tetanus antitoxin and crying out because of severe abdominal pain by 9:00 p.m.; refused all fluids by mouth. At 11:30 p.m. 500 cc 10% glucose in saline containing 4 grams vitamin C. September 5th. Attacks of muscle spasm more severe than at any other time. 12:00 midnight, 600,000 units procaine penicillin and 4 grams vitamin C; same amount of the vitamin at 4:00 a.m. and 8:00 a.m. Fairly normal sleep from 3:00 a.m. to 7:00 a.m. At 9:00 a.m. 300,000 units T.A.T. in saline intravenously; severe convulsive-like seizures of abdominal and back muscles reported at 11:00 a.m. 12:00 noon 4 grams vitamin C; sleeping quietly by 1:00 p.m. Oil retention enema given at 2:00 p.m. but unable to retain. Because of very severe seizures in which patient's body arched off the bed which was accompanied by profuse sweating we decided that if our little patient was to live some NEW type therapy must be adopted. Accordingly, 200 mgm of Tolserol in 500 cc D5 in water was started, the flow being 35 drops per minute. (This was an experimental dose since we could find no reports on the use of Tolserol intravenously in children.) 8:00 p.m. 4 grams vitamin C and 30,000 units tetanus antitoxin in saline at 9:00 p.m. Crying because of severe abdominal pain at 10:30 p.m.; also very restless and absolutely unable to swallow. September 6th. 12:00 midnight, 4 grams vitamin C and 600,000 units procaine penicillin. No response was observed after 6 hours with the 200 mgm. of Tolserol, so we elected to give 800 mgm. Tolserol in 500 cc D5 in water at this time, employing the 35 drops per minute schedule. 1:00 a.m. patient was resting quietly; asleep at 1:30 a.m. This continued until bath at 7:00 a.m. except for an occasional interruption caused by asking the patient how he felt. This was done to evaluate the degree of relaxation present; each time he responded gently that he was "feeling fine" and then returned to his slumbers. Vitamin C now given at 12-hour intervals maintaining the same dose

schedule. 12:45 p.m. 20,000 units T.A.T in 5% glucose in water and at 9:00 p.m. 28,000 units tetanus antitoxin in saline, both intravenously. It was of great significance to note that this time there were no exacerbations of muscle spasms—the Tolserol was doing a good job. September 7th was relatively uneventful. Three cc aqueous solution adrenal cortex was given every 8 hours for three times to relieve the strain on this gland. 5:00 p.m., we really began to hear from our tetanus antitoxin as the first urticarial wheel appeared on patient's right forearm. Benadryl 10 mg. and Kutapressin $\frac{1}{2}$ cc were given intramuscularly; one hour later 20 mgm benadryl and 3 mm adrenalin. Calamine lotion with phenol to whelps which by 9:00 p.m. had covered the entire body. Adrenalin 3 mm and benadryl 10 mg were given every 30 to 60 minutes, alternating, until 2:00 a.m. following day. Calcium gluconate 10 cc given intravenously. In spite of this therapy the stimulation from this serum reaction was enough to re-excite the muscles into painful spasms. At 11:30 p.m. 1000 mgm Tolserol in 500 cc 5% glucose in water was started. It was a rough night. By 3:00 a.m. the Tolserol was taking hold and "all was well" by 6:00 in the morning. Following this episode streptomycin was substituted for the penicillin in the light that it, too, might have played a part in the allergy. From this time until discharge Kutapressin, benadryl, and B-Complex were employed freely. Intradermal tetanus toxoid was given daily the last five days in the hospital. From this day on nourishment was taken freely when offered and muscle pain and spasm was absent. He was discharged on the 18th hospital day but could have safely returned home 10 days before. This we did not know at the time.

Vitamin C was employed for the following reasons: (1) Its antihistamine like action; (2) For its diuretic effect; (3) For its ability to neutralize exotoxins; (4) For its role in antibody formation. It is interesting to note that on September 8th, 10 days before discharge, the white blood count was 4,800 and the differential showed 45% lymphocytes and 55% polymorphs. Kracke states that one of the most notable instances of the increase of lymphocytes above normal is in recovery from acute infections. Kracke reports that Wintrobe gives as a fact: "That the lymphocytes are active in antibody formation."

In summary the following schedule will serve well in the treatment of TETANUS: (1) A debridement if a "ragged" wound is present; (2) Clean the field well. Any good antiseptic, applied thoroughly, will serve to sterilize the field. (Ether is too seldom used. It will destroy most bacteria, even colon bacillus, without injuring protoplasm.) Sterilizing of the wound when present, is done, not so much against the bacillus tetani which is highly resistant but for the destruction of other pathogenic or even non-pathogenic organisms: Park and Williams report that it has been found that pure cultures of tetanus, after the germs have sporulated and the toxins been destroyed by heat, can be injected into animals without producing tetanus. But if pathogenic strepto-cocci or staphylococci or even non-pathogenic organisms are injected simultaneously with the spores, or if there is an effusion of blood at the point of injection, or if there was a previous or later bruising of the tissues, the animals surely die of tetanus. The spores under such conditions can develop and produce the disease. For this reason one should give 75,000 units antitoxin deep intramuscularly above the wound when present and when possible. (3) Intravenous fluids; (4) intradermal tetanus toxoid 0.1 cc for five consecutive days; (5) massive doses of vitamin C around the clock and given by needle; (6) intravenous

Tolserol in adequate amounts. In our case 1000 mgm for a body weight of 20 Kg. was adequate. One can only hope that all the states will adopt legislation requiring annual booster injections of tetanus toxoid for all people regardless of age. This to be given at the expense of the states with the co-operation of its practicing physicians.

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The authors, in Australia, cite the work of Irwin Stone's *The Healing Factor: Vitamin C Against Disease* (1972) and Dr. Fred R. Klenner's 1957 article, "The Black Widow Spider: Case History" (pp. 103-108 in this volume), regarding the use of injectable vitamin C in treating bites from a variety of venomous creatures. The authors call for more research on the use of vitamin C as a "non-specific antitoxin." Clinical data supporting vitamin C's use as an antidote appears in *You Can't Live without Vitamin C*, (1979) written by Phyllis Cilento, the article's lead author. —R.D.M.*

Venomous Bites and Vitamin C Status

Phyllis Cilento, Archie Kalokerinos, Ian Dettman and Glen Dettman, Australia
The Australian Nurses Journal, May 1980, p. 19

Like most concerned Australians we followed the tragic fight for life at the Royal Alexandra Hospital for Children in Sydney of 2 1/2-year-old Jamie Cullie: bitten by a funnel-web spider. Jamie died.

Dr. Struan Sutherland of the CSL, whose excellent work we acknowledge, says that many more people will die of funnel-web spider bites, despite efforts to develop an antidote. He further says that it was unlikely that any single drug would provide the answer and that they would check new drugs as they came on the market to try to find a more effective combination.¹

In his book, "The Healing Factor", Dr. Irwin Stone of San Jose, USA documents research undertaken not only into the prevention of spider bite mortalities but other venomous creatures.² In yet a further book, written by one of us³ clinical data and historical facts supporting Stone's data are outlined.

More specifically, Dr. Frederick Klenner, of North Carolina, USA, published a comprehensive paper on treatment of the Black Widow spider bite in the *Tri State Medical Journal*.⁴

Klenner claims that he treated eight cases of such bites during his tenure as a physician, all successfully. He appeals to others to use this powerful therapeutic agent.

The powerful therapeutic agent's name? ... ascorbate, or as it is perhaps erroneously referred to as "Vitamin C".

Please wait, don't pull down the shutters of prejudice without some fair trials.

Klenner emphasises that to obtain optimum results the treatment must be given as soon as possible and sufficient ascorbate must be used.

In the case of the Black Widow spider, Klenner suggests 350 mg per kg body weight be given intravenously in conjunction with a single dose of calcium gluconate. This treatment may be used alone or in support of currently recommended regime.

Editor's note: More than 50,000 people per year die worldwide from poisonous snake-bite.

As ascorbate is a non toxic, non specific antitoxin it may be used for any type of venomous bite without having to await identification of the culprit.

Some of the papers mentioned by Stone² demonstrate that animals have been protected from anaphylactic shock by first giving them sufficient 'vitamin C'.

It must therefore be advantageous for those journeying high risk 'bite' areas (and that would include most of us) to ensure that they are 'primed' against the initial shock by taking grams of ascorbate instead of mgms of 'vitamin C'.

We are confident that once trials are made, then the prediction by one of us (P.C.) that a 'vitamin C' anti-toxin kit would soon be a necessary part of equipment in the following will become a reality:

The doctors bag, and surgery.

The casualty department of hospitals, particularly in the country.

The ambulance.

First aid stations and life saving clubs.

Professionals and parents will then be relieved of the anxiety and helplessness they are often confronted with.

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This important study was conducted in Bangladesh, where at the time of the research tetanus accounted for 26 percent of all infant deaths. Sixty-two tetanus patients aged 1 to 12 years and 55 patients aged 13 to 30 years received conventional antitetanus therapy. Additionally, 31 members of the younger group and 27 of the older group received injections of 1 gram of ascorbic acid daily as a supplement to conventional therapy. In the younger group receiving vitamin C, zero percent died, while 74 percent of those who did not get the injections failed to survive. In the older group, 37 percent of those who got the vitamin C died, while 68 percent of those who did not get the vitamin C succumbed. Injections of vitamin C were also found to protect two-day-old chicks from induced strychnine poisoning.—*R.D.M.**

Effect of Ascorbic Acid in the Treatment of Tetanus

K. Jahan, K. Ahmad and M.A. Ali, University of Dhaka and Infectious Disease Hospital, Mohakhali, Dhaka
Bangladesh Med. Res. Counc. Bull., June 1984, pp. 24-28

SUMMARY

The effect of daily intravenous administration of 1,000 mg ascorbic acid (AA) in tetanus patients aged 1-30 years was studied. In the age group of 1-12 years, 31 patients were treated with AA as additional to antitetanus serum, sedatives and antibiotics. It was found that none of the patients died who received AA along with the conventional antitetanus therapy. On the other hand, 74.2 per cent of the tetanus patients who received the conventional antitetanus therapy without AA (control group) were succumbed to the infection. In the other age group of 13-30 years, there were 27 and 38 patients in the treatment and control groups respectively. The mortality in the AA and control groups were 37 percent and 67.8 percent respectively.

*Editor's note: For those who insist on hard-nosed data before admitting the efficacy of injectable vitamin C, this study from Bangladesh should be an eye-opener. In 1937, Claus W. Jungeblut of Columbia University reported that vitamin C could neutralize tetanus toxin in guinea pigs ("Inactivation of Tetanus Toxin by Crystalline Vitamin C (l-Ascorbic Acid). [*Journal of Immunology* 1937. Vol. 33: 203-214]). By 1954, Dr. Fred Klenner was using injectable vitamin C to treat tetanus in his medical practice (see Klenner's 1954 article on pp.87-94 of this volume). In effect, Jungeblut's 1937 results with animals were confirmed by Dr. Klenner in his medical practice. This research from Bangladesh validates Jungeblut and Klenner's finding in a rigorous medical trial using a control group.

Perhaps it is worth quoting from Jungeblut's 1937 report: "It must be concluded that vitamin C, as far as its in vitro action is concerned, cannot be regarded as a specific detoxicant for any given virus or toxin, but rather as a substance which acts indiscriminately against a variety of toxins and viruses" (p. 212). Obviously, the potential cost-benefit ratio of more research into and wider use of injectable vitamin C by mainstream medicine is too great to continue to ignore, especially in a world overflowing with medical need.

These results suggest that AA might play an important role in reducing the mortality of tetanus. This was supported by the fact that AA was found to mitigate the toxic effects of strychnine producing tetanus like condition in young chicks in the present study.

INTRODUCTION

While tetanus is no longer a problem in advanced countries as almost every body is immunized, it has remained a dreaded disease and a major killer in countries like Bangladesh. The neonatal death rate due to tetanus is estimated to be 24.05 per thousand live births and accounts for 26.20 per cent of all infant deaths (Islam, 1983). Considerable cases are also seen in older children and adults arising out of injuries while playing or working in the fields. There are incidents of the disease due to circumcision or surgical procedures where sterile condition is not maintained. However, the mortality of tetanus is high in rural areas where adequate treatment is hardly available. Even in the urban hospitals, mortality due to tetanus neonatorum is believed to be 80 to 90 per cent and in adult cases it is over 60 per cent (Infectious Disease Hospital Record, 1983). The conventional antitetanus therapy includes antitetanus serum, sedatives, antibiotics, muscle relaxant and sometimes steroids. But the role of AA in the therapy of tetanus has not been previously investigated.

It has been observed that β -N- ϵ oxalyl diaminopropionic acid (ODAP) isolated from lathyrus sativus (known as Khesari in local language) (Rao et al, 1964) was found responsible for neurolathyrism (Sarma and Padmanaban, 1969). It was also observed that in both tetanus and in neurolathyrism some common characteristics such as spastic paralysis and neuroexcitation are seen. Both ODAP and tetanus toxin find their way to the central nervous system (CNS) to get themselves attached to the synaptosomes (Lakshmanan and Padmanaban, 1977). Glutamic acid also under certain circumstances has been found to affect the CNS in the way ODAP does (Olney et al, 1976). Both ODAP and glutamate are considered to have common receptors (Lakshmanan and Padmanaban, 1977). It was found that biological effect of ODAP as well as glutamate was related to the serum level of AA and in fact both neurolathyrism and glutamate toxicity could be prevented by administration of AA (Ahmad and Jahan, 1983).

On the basis of the above fact, it was considered that AA might have some beneficial effects in the treatment of tetanus. The present study was therefore, undertaken to validate the above concept.

MATERIALS AND METHODS

A total number of 117 tetanus patients admitted into the Infectious Disease Hospital, Mohakhali, Dhaka were studied. They were divided into two different age groups. In the age group of 1-12 years, there were 31 patients in the treatment group who received 1000 mg. AA daily in addition to conventional antitetanus therapy which included antitetanus serum, sedatives, antibiotics and muscle relaxant etc. There were also 31 patients in the similar age groups who received only the conventional antitetanus therapy but no AA and this group served as control. In the other age group of 13-30

years, there were 27 and 28 patients in the treatment and control groups respectively and they were treated in a similar manner as in the age group of 1-12 years.

In view of the recognised similarity between the mode of action of tetanus toxin and strychnine, (Heyningen et al, 1971) an animal experiment was conducted in the Institute of Nutrition and Food Science, University of Dhaka to investigate whether AA could mitigate the toxicity induced by strychnine. Two-days old chicks weighing 32-35 gm were divided into four groups with 15 birds in each group. Birds of group I were received 5 µg of strychnine sulphate only and those of in group II received strychnine sulphate in the same dosage along with 30 mg AA 10 minutes before strychnine. Birds of group III were administered strychnine in a higher dosage of 10 µg only and the group-IV received both strychnine (10µg) and AA 30 mg. Both the drugs were administered intraperitoneally in aqueous solutions.

RESULTS

The effect of AA in the treatment of tetanus was shown in Table I. In the age group of 1-12 years, there was no mortality in patients who received 1000 mg AA daily (i.v.) in addition to conventional antitetanus therapy. On the other hand, in the control group i.e. the patients who had not received AA along with antitetanus therapy, the mortality rate was 74.2 per cent (Table-I). In another age group of 13-30 years, addition of AA to the conventional antitetanus regimen caused a marked reduction in the mortality [should be mortality per ed.]. In the treatment group (i.e. patients that received both AA and antitetanus therapy), the mortality was only 37 percent as opposed to 67.8 per cent in patients who had not received AA (Table-I).

The results of animal experiments are shown in Table-II. Administration of AA protected the chicks from strychnine toxicity and the chicks who received AA and strychnine did not develop the signs of strychnine toxicity indicating that AA mitigated the same.

DISCUSSION

The results of the present study indicate that AA acts in some way to mitigate the toxicity of tetanus toxin so that in the age groups of 1-12 years none of the patient receiv-

TABLE I
Studies on the effect of daily administration of (i.v.) 1000 mg of AA as supplement to conventional treatment on the recovery of tetanus patients

Age group (years)	Patients receiving ascorbic acid			Patients not receiving ascorbic acid		
	No. of Patients	Patients who Recovered	Mortality	No. of Patients	Patients who Recovered	Mortality (percentage)
1-12	31	31	00%	31	8	74.2
12-30	27	17	37%	28	9	67.8

TABLE II
Effect of AA on the toxicity of strychnine sulphate (SS) in chicks

Groups	Dose of SS per chick (μ g)	Dose of AA per chick (mg)	Observation
I	5	—	Wings of all birds stretched. Some walked on toes, others kept jumping and they could not walk.
II	5	30	No symptoms.
III	10	—	Extensor paralysis of legs, opisthotonus and severe convulsion. All but three died.
IV	10	30	Extensor paralysis in 3 chicks. No neurological symptoms in others. The affected birds recovered in about 30 minutes after the appearance of the symptoms.

The number of birds were 15 in each group.

ing AA succumbed to the toxinoses of tetanus as opposed to the corresponding control groups. In the other age group of 13-30 years, although some succumbed but there was substantial reduction in mortality due to the addition of AA. Even though several variables such as site injury, status of infection before start of treatment, nutritional status of the patients and exposure to risks of secondary infection must also have acted as determinants of mortality amongst tetanus patients, the beneficial effect of AA as seen in this study appears significant.

During the course of study, it was noticed that patients succumbed to tetanus even three to four weeks after admission. This is contrary to the literature report that death if it occurs follows relatively soon after the appearance of symptoms, the dictum of Hippocrates, such persons as are seized with tetanus die within four days or if they pass those they recover, still stands (cited by Burrows, 1968). In many instances it would appear that those patients had almost recovered when fresh wave of convulsions would overtake bringing the end.

The studies on human patients of tetanus and the studies on strychnine toxinoses in chicks indicate that AA interacts with tetanus toxin as well as strychnine to reduce their toxic effect although the mechanism of this interaction is yet to be understood.

ACKNOWLEDGEMENTS

The authors acknowledge the cooperation and management of the clinicians of the Infectious Disease Hospital during the course of this study. The authors are also

thankful to Professor Nurul Islam, Director and Professor of Medicine, Institute of Postgraduate Medicine and Research, Dhaka for encouragements.

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In 1949, Dr. Fred Klenner stood up at a meeting of the American Medical Association and described how he had treated and cured 60 cases of polio during the epidemic that year. Massive frequent injections of vitamin C were used, he said, to produce the cure. An abstract of his remarks was published in the *Journal of the American Medical Association*. The author of this article discusses the medical profession's response—or lack of it—to Dr. Klenner's announcement and offers some suggestions as to why an apparent cure for so many diseases has been ignored for more than half a century, essentially never having come up on scientific medicine's radar screen.—*R.D.M.*

The Origin of the 42-Year Stonewall of Vitamin C

Robert Landwehr, Berkeley, CA,
Journal of Opthomolecular Medicine, 1991, vol. 6, no. 2, pp. 99-103.

In the late spring of 1949 the United States was in the grip of its worst poliomyelitis epidemic ever. On June 10 a paper on ways to save the lives of bulbar polio victims was read at the Annual Session of the American Medical Association (subsequently printed in its journal, *JAMA*, September 3, 1949, pages 1-8, volume 141, no. 1). Following the talk members of the audience were invited to comment. The first speaker, a leading authority from Pasadena, focused on details of tracheotomy techniques caused when paralyzed breathing, swallowing and coughing muscles of victims threatened their lives. Why the next person was recognized is puzzling. The only national recognition he had received—and it was obviously very limited—was that his picture appeared in *Ebony* in 1947 for having delivered of a deaf-mute black woman the first known surviving, identical quadruplets in the country. Here is the abstract of his remarks as recorded in *JAMA*:

“Dr. F. R. Klenner, Reidsville, N.C.: It might be interesting to learn how poliomyelitis was treated in Reidsville, N.C., during the 1948 epidemic. In the past seven years, virus infections have been treated and cured in a period of seventy-two hours by the employment of massive frequent injections of ascorbic acid, or vitamin C. I believe that if vitamin C in these massive doses—6,000 to 20,000 mg in a twenty-four hour period—is given to these patients with poliomyelitis none will be paralyzed and there will be no further maiming or epidemics of poliomyelitis.”

The discussion period was, of course, to be devoted to hearing relevant comments of the world's leading authorities on the treatment of bulbar polio symptoms, not to airing another claim of a cure. One can imagine the silence that must have greeted this sweeping, out-of-place declaration by a small-town general practitioner. Four other speakers, three more bulbar experts and an anesthesiologist, followed. None referred to Dr. Klenner's remarks.

The empirical, clinical basis for Klenner's statement is found in his paper “The Treatment of Poliomyelitis and Other Virus Diseases with Vitamin C”, published in the

July 1949 issue of the *Journal of Southern Medicine and Surgery*. On pages 211-212 he writes:

“In the poliomyelitis epidemic in North Carolina in 1948, 60 cases of this disease came under our care. These patients presented all or almost all of these signs and symptoms: Fever of 101 to 104.6°, headache, pain at the back of the eyes, conjunctivitis, scarlet throat; pain between the shoulders, the back of the neck, one or more extremity, the lumbar back; nausea, vomiting and constipation. In 15 of these cases the diagnosis was confirmed by lumbar puncture; the cell count ranging from 33 to 125. Eight had been in contact with a proven case; two of this group received spinal taps. Examination of the spinal fluid was not carried out in others for the reasons: (1) Flexner and Amoss had warned that ‘simple lumbar puncture attended with even very slight hemorrhage opens the way for the passage of the virus from the blood into the central nervous system and thus promotes infection.’ (2) A patient presenting all or almost all of the above signs and symptoms during an epidemic of poliomyelitis must be considered infected with this virus. (3) Routine lumbar puncture would have made it obligatory to report each case as diagnosed to the health authorities. This would have deprived myself of valuable clinical material and the patients of most valuable therapy, since they would have been removed to a receiving center in a nearby town.

The treatment employed was vitamin C in massive doses. It was given like any other antibiotic every two to four hours. The initial dose was 1,000 to 2,000 mg, depending on age. Children up to four years received the injections intramuscularly. Since laboratory facilities for whole blood and urine determinations of the concentration of vitamin C were not available, the temperature curve was adopted as the guide for additional medication. The rectal temperature was recorded every two hours. No temperature response after the second hour was taken to indicate the second 1,000 or 2,000 mg. If there was a drop in fever after two hours, two more hours was allowed before the second dose. This schedule was followed for 24 hours. After this time the fever was consistently down, so the drug was given 1,000 to 2,000 mg every six hours for the next 48 hours. All patients were clinically well after 72 hours. After three patients had a relapse the drug was continued for at least 48 hours longer—1,000 to 2,000 mg every eight to 12 hours. Where spinal taps were performed, it was the rule to find a reversion of the fluid to normal after the second day of treatment.

For patients treated in the home the dose schedule was 2,000 mg by needle every six hours, supplemented by 1,000 to 2,000 mg every two hours by mouth. The tablet was crushed and dissolved in fruit juice. All of the natural “C” in fruit juice is taken up by the body; this made us expect catalytic action from this medium. Rutin, 20 mg, was used with vitamin C by mouth in a few cases, instead of the fruit juice. Hawley and others have shown that vitamin C taken by mouth will show its peak of excretion in the urine in from four to six hours. Intravenous administration produces this peak in from one to three hours. By this route, however, the concentration in the blood is raised so suddenly that a transitory overflow into the urine results before the tissues are saturated. Some authorities suggest that the subcutaneous method is the most conservative in terms of vitamin C loss, but this factor is overwhelmingly neutralized by the factor of pain inflicted.

Two patients in this series of 60 regurgitated fluid through the nose. This was inter-

puted as representing the dangerous bulbar type. For a patient in this category postural drainage, oxygen administration, in some cases tracheotomy, needs to be instituted, until the vitamin C has had sufficient time to work—in our experience 36 hours. Failure to recognize this factor might sacrifice the chance of recovery. With these precautions taken, every patient of the series recovered uneventfully within three to five days.”

This paper is quoted at length to allow readers to judge for themselves whether or not Dr. Klenner made up all these details. In subsequent publications he gave details about curing life-threatening polio cases, and described his general procedures in his paper “The Vitamin and Massage Treatment for Acute Poliomyelitis”, appearing in the *Journal of Southern Medicine and Surgery* in August, 1952.

One of the reasons why Klenner’s declaration at the AMA annual session was undoubtedly met with silence was that since 1939 polio experts were quite certain that vitamin C was not effective against polio. There seemed little doubt that Dr. Albert B. Sabin, a highly respected figure in medical research even before he developed his successful vaccines, had demonstrated that vitamin C had no value in combatting polio viruses. In 1939 he published a paper showing that vitamin C had no effect in preventing paralysis in rhesus monkeys experimentally infected with a strain of polio virus. He had tried to corroborate the work of Dr. Claus W. Jungeblut, another highly respected medical researcher, who had published in 1935 and 1937 papers indicating that vitamin C might be of benefit. Sabin could not reproduce Jungeblut’s results even though he consulted Jungeblut during the course of the experiments. It seemed to be a fair trial, and Sabin’s negative results virtually ended experiments with vitamin C and polio.

How then could a Dr. Fred R. Klenner, a virtually unknown general practitioner specializing in diseases of the chest, from a town no one ever heard of, with no national credentials, no research grants and no experimental laboratory, have the nerve to make his sweeping claim in front of that prestigious body of polio authorities?

Around 1942 Klenner’s wife suffered bleeding gums and her dentist recommended pulling out all her teeth. Dr. Klenner thought that solution too Draconian and remembered reading about research using vitamin C to cure chimpanzees with a similar problem. He gave her several injections of the vitamin and the bleeding stopped. Soon after, this dramatic result encouraged him to try vitamin C on an obstinate man who was near death from viral pneumonia. Klenner described this seminal experience in a 1953 paper “The Use of Vitamin C as an Antibiotic.”

“Our interest with vitamin C against the virus organism began ten years ago in a modest rural home. Here a patient who was receiving symptomatic treatment for virus pneumonia had suddenly developed cynosis. He refused hospitalization for supportive oxygen therapy. X-Ray had not been considered because of its dubious value and because the nearest department equipped to give such treatment was 69 miles distant. Two grams of vitamin C was given intramuscularly with the hope that the anaerobic condition existing in the tissues would be relieved by the catalytic action of vitamin C acting as a gas transport aiding cellular respiration. This was an old idea; the important factor being that it worked. Within 30 minutes after giving the drug (which was carried in my medical bag for the treatment of diarrhea in children) the characteristic breathing and slate-like color had cleared. Returning six hours later, at eight in the evening, the patient was found sitting over the edge of his bed enjoying a late dinner. Strangely

enough his fever was three degrees less than it was at 2 p.m. that same afternoon. This sudden change in the condition of the patient led us to suspect that vitamin C was playing a role of far greater significance than that of a simple respiratory catalyst. A second injection of one gram of vitamin C was administered, by the same route, on this visit and then subsequently at six hour intervals for the next three days. This patient was clinically well after 36 hours of chemotherapy. From this casual observation we have been able to assemble sufficient clinical evidence to prove unequivocally that vitamin C is the antibiotic of choice in the handling of all types of virus diseases. Furthermore it is a major adjuvant in the treatment of all other infectious diseases.”

Again this paper is quoted at length to allow readers to judge for themselves whether or not the author made this up or deluded himself in some way. From 1943 through 1947 Dr. Klenner reported successful treatment of 41 more cases of viral pneumonia using massive doses of vitamin C. From these cases he learned what dosage and route of administration—intravenously, intramuscularly, or orally—was best for each patient. Dr. Klenner gave these details in a February 1948 paper published in the *Journal of Southern Medicine and Surgery* entitled “Virus Pneumonia and Its Treatment with Vitamin C”. This article was the first of Dr. Klenner’s twenty-eight (through 1974) scientific publications.

Klenner realized, of course, that vitamin C’s effectiveness with viral pneumonia opened up the possibility of curing other viral diseases. “With a great deal of enthusiasm,” in Klenner’s phrase, he tried its effectiveness with all of the childhood diseases, particularly measles. By the spring of 1948, when a measles epidemic came to Reidsville, Klenner was so confident of vitamin C’s efficacy with these diseases that he devised what would ordinarily be an outrageous experiment with his two little daughters. He had them play with children known to be in the contagious phase of measles. When the usual syndrome of measles had developed and his daughters were obviously sick, vitamin C was started. Again Klenner’s words from his 1953 paper:

“In this experiment it was found that 1,000 mg every four hours, by mouth, would modify the attack. Smaller doses allowed the disease to progress. When 1,000 mg was given every 2 hours all evidence of the infection cleared in 48 hours. If the drug was then discontinued for a similar period (48 hours) the above syndrome returned. We observed this off and on picture for thirty days at which time the drug (vitamin C) was given 1,000 mg every 2 hours around the clock for four days. This time the picture cleared and did not return.”

With this background of experiences—with human beings, not experimental animals—Klenner gained confidence in and control over his vitamin C treatment.

One reason he turned his attention early to treating measles was that he knew that measles viruses were about as small as polio viruses and he hoped massive doses of vitamin C would be effective against the dreaded Crippler. By 1948 he was ready to treat polio with vitamin C, and in that year North Carolina suffered its worst epidemic ever—2,518 new cases. Dr. Klenner’s hopes were realized when, as has been related above, he cured sixty patients with massive frequent injections of vitamin C.

With seven years of experience behind him one can understand not only why Dr.

Klenner had the nerve to speak up on June 10, 1949 but why he undoubtedly felt morally obligated to do so.

After 1949 polio epidemics continued to take their terrible toll. The peak year for The Crippler in the U.S. was 1952—57,628 cases. During the 1950s isolated doctors around the world tried Klenner's cure. Those who used vitamin C at doses below those recommended by Klenner reported no benefit; those who followed his dosages reported good results. Dr. H. Bauer of the University of Switzerland Clinic, Basel in 1952 reported benefits to his polio patients with 10 to 20 grams of vitamin C per day. Dr. Edward Greer, using doses in Klenner's recommended range of 50 to 80 grams per day, recorded in 1955 good clinical results with five serious cases of polio. Dr. Abram Hoffer recalls that a controlled study, conducted in Great Britain in the late 50s with 70 young polio victims, confirmed Klenner's cure. All those given vitamin C recovered completely, while a significant number of those not given vitamin C suffered some permanent damage. (This study was not published because of the success of the polio vaccines.) Dr. Klenner himself reported that he received scores of letters from doctors in the U.S. and Canada corroborating his striking results. Some of the letters described how they cured their own children, others, how the doctors had cured themselves.

What kind of reception did Dr. Klenner's discoveries receive from the medical establishment? There are two references to Klenner's 1949 paper in national, mainstream publications. The title of that paper was included in the October 7, 1949 issue of the *Current List of Medical Literature*, published by the U.S. Army Medical Library. The paper was also included in the second edition of *A Bibliography of Infantile Paralysis—1789-1949*, published in 1951 and prepared under the direction of the National Foundation for Infantile Paralysis. Instead of abstracting the paper in the usual manner, it printed only Dr. Klenner's last paragraph, which was not a summary but an obvious rhetorical statement Klenner felt necessary to counter the skepticism he knew would greet his quick, inexpensive cures. Other than these two references, mainstream medical publications made no mention of Klenner and his work. One of *JAMA's* regular departments was Current Medical Literature, in which its editors abstracted papers they considered of special note. Many polio papers were abstracted in 1949, but not Klenner's.

The National Foundation for Infantile Paralysis was founded in 1938 by polio's most famous victim, President Franklin Roosevelt, to raise money through the March of Dimes to combat the disease. Most polio research was funded by the National Foundation. There is no mention of Dr. Klenner's work or of vitamin C's possible benefits to polio victims in any of the Foundation's annual reports. Not one dime was spent to prove or disprove Klenner's claim. Before 1949 a claim of a cure was promptly looked into and money spent until it was proved false. But with Klenner's claim nothing happened.

It was certainly not for lack of research funds that nothing happened. John M. Russell, in the 1960 book *The Crisis in American Medicine*, edited by Marion K. Sanders, described the glut and waste of money for medical research in the 1950s. Russell points out that the public clamor for a cure for polio was so great that in 1954 Congress appropriated \$1,000,000 specifically earmarked for polio research. It turned out that there was so much polio money floating around that the recipient of this largess, the

U.S. Public Health Service, classified such unlikely diseases as hepatitis as “poliolike” so that none of this money would have to be returned to the U.S. taxpayer.

Five International Poliomyelitis Congresses were convened every three years from 1948 to 1960 to deal with the polio epidemics around the world. In all of the voluminous reports of these conferences there is no reference to Klenner or to vitamin C. Only the first congress dealt briefly with the possible effect of nutrition, and this was dismissed by the statement of an expert “that no clinical evidence is known to me which justifies an increase in intake of vitamins beyond usual recommended allowances”.

Thus in 1949 the polio experts at the Annual Session of the AMA knew of Klenner’s claim, as did the many readers of *JAMA*’s lead article of its September 3 issue, the many researchers who used the National Foundation’s *Bibliography*, those that kept up with the titles in the *Current List of Medical Literature*, and the relatively few readers of the *Journal of Southern Medicine and Surgery*. All this exposure led to no official inquiry or follow-up of Dr. Klenner’s work by U.S. government health authorities or the National Foundation. No one in authority anywhere stepped forward to insist that it be checked out. The strategy of medical leaders—conscious or unconscious, planned or unplanned—was clearly to ignore Dr. Klenner and hope his claims would be forgotten.

It worked. Klenner’s cure never became well known and today has sunk almost into oblivion. A synopsis of polio infection and research by Ernest Kovacs entitled “The Biochemistry of Poliomyelitis Viruses”, published in 1964, makes no reference to Klenner. In 1985 Friedrich Koch and Gebhard Kock published *The Molecular Biology of Poliovirus*. It contains in its opening chapter a history of the disease, but it says nothing about Klenner, or even about the extensive vitamin C research done by Drs. Jungeblut and Sabin with monkeys in the 30s. It’s as though polio–vitamin C research never happened.

To this day it is mainstream medicine’s position that there is no cure for polio. The Encyclopedia American quotes Richard W. Price of Memorial Sloan-Kettering Cancer Center of New York City: “No specific treatment is effective once neurological involvement becomes manifest.” A thoroughly exasperated Klenner concluded a February 1959 paper in the *Tri-State Medical Journal* with these words:

“Should the disease be present in the acute form, ascorbic acid given in proper amounts around the clock, both by mouth and needle, will bring about a rapid recovery. We believe that ascorbic acid must be given by needle in amounts from 250 mg to 400 mg per kg body weight every 4 to 6 hours for 48 hours and then every 8 to 12 hours. The dose by mouth is the dose that can be tolerated. To those who say that Polio is without cure, I say that they lie. Polio in the acute form can be cured in 96 hours or less. I beg of someone in authority to try it.”

Today there are areas of the world where polio vaccine is still not used and where the incidence of polio is increasing. Polio remains The Crippler, and the only effort of the World Health Organization is to increase vaccination. The leading medical authorities—the editors of the leading journals, the heads of the AMA and the National Foundation, U.S. Surgeons-General and the heads of other U.S. governmental health agencies—were, and are, responsible for stonewalling for 42 years Dr. Klenner’s simple, inexpensive cure for many viral diseases, including the dreaded polio.

1949—a year in medicine which will live in infamy.

Massive Doses of Vitamin C In the Treatment of Viral Diseases

WILSON L. DALTON, M.D.
Shelbyville

TREATMENT OF VIRAL DISEASES presents to the physician a perplexing and frequently unrewarding problem, particularly since some 50 different diseases of man are of viral etiology. To date no generally effective therapeutic measures have been devised for treating viral diseases, although some diseases caused by the largest of the known viruses appear to be affected by some chemotherapeutic agents. Therapy with specific antisera is useful as a preventive measure during the incubation period of some viral diseases, but is generally of little value once clinical manifestations of the infection have ensued.¹ Therefore, an effective therapeutic agent that would substantially reduce the morbidity of the majority of viremias would provide the physician with a most valuable adjunct to treatment.

There have been a number of reports in the literature suggesting that infectious disease processes rapidly accelerate vitamin C depletion and greatly increase vitamin C requirement.² The role of vitamin C in maintaining stability and tensile strength of connective tissue is well known. This property favors, among other things, the building of a protective barrier against infectious invasion.⁴ When ascorbic acid stores are severely depleted during the course of infectious diseases, capillary resistance decreases and susceptibility to the action of certain toxins appears to increase.² It has been suggested that means of altering the susceptibility of cells to invasion by viruses could provide a method of controlling as well as preventing infection.⁷

Several investigators have reported employing massive parenteral doses of ascorbic acid in the adjunctive treatment of viral diseases. Klenner³ has advocated and employed massive doses of intravenous ascorbic

acid for many years in the treatment of various viral diseases including measles, mumps, chickenpox, viral pneumonia and viral encephalitis, and has reported remarkable results. Even with doses as high as 65 mg./Kg. Klenner rarely encountered any adverse effects and those were limited to the site of injection. Klenner has administered chemotherapeutic agents along with ascorbic acid to reduce secondary bacterial infection and has recommended the subsequent use of Vitamin B₁ following infectious diseases involving the nervous system. He further theorizes that the near absence of ascorbic acid in infectious states may be attributed to the vitamin combining with the toxin and/or virus to form a new complex which is easily destroyed by oxidation.

Free from Reaction

McCormick⁴ administered ascorbic acid intravenously or intramuscularly in massive repeated doses, 500 to 1000 mg. every four hours. He reported that this approach exhibited a potent chemotherapeutic-like action in acute infectious processes which compared favorably to that of the sulfonamides or antibiotics but with the advantage of complete freedom from toxic or allergic reactions. Baur and Staub⁵ reported highly satisfactory results were obtained with daily intravenous infusions of 10 gm. of ascorbic acid in 1000 cc. of isotonic saline solution administered for an average of five days to patients with infectious hepatitis. They have described the action of ascorbic acid as "virucidal." Calleja and Brooks⁶ reported that daily intravenous infusion of 5 gms. of ascorbic acid for 24 days resulted in remarkable improvement in a patient with acute hepatitis when other therapeutic measures had proved futile.

Reports from German literature show

that high doses of vitamin C are beneficial in epidemic hepatitis in children. These beneficial effects were clearly observed in 63 cases of epidemic hepatitis treated with high doses of vitamin C in doses of 10 gms. daily for an average of five days given either by rectal infusion or intravenously, or both.⁹

This investigator evaluated a product trademarked Viron-1* as an adjunct in the treatment of a series of cases involving diseases of probable viral etiology. Viron is a preparation for intravenous administration consisting of 2000 mg. of ascorbic acid per dose fortified with certain B-vitamins. I was primarily concerned with patient response to this mode of therapy since time of recovery was of major economic importance to these patients. It has been my past experience that the more intense the patient's symptoms the greater the morbidity and the longer the convalescent period.

The following case histories are representative of this therapeutic regime:

Infectious Hepatitis

A 20-year-old white female hospital medical technician was first seen for the present illness on Nov. 9, 1959. The illness dates back to the spring of 1959 when she began to feel progressively weaker, exhibited malaise, anorexia, slight nausea, when it was discovered that she had an icteric tinge in her serum. She was treated with bed rest for four days and the sub-clinical jaundice disappeared with a return of her icterus index to normal.

Later in November her symptoms of malaise were intensified, she began to lose weight, became progressively weaker, and presented herself for examination. It was decided that she had clinical jaundice of a minor degree; however, the liver was not palpable and her physical examination was essentially normal.

She was hospitalized on Nov. 11 and was seen in consultation by an internist who confirmed the diagnosis of hepatitis, etiology unknown. Her admission laboratory work revealed a urine which was essentially

negative, except for the presence of bile. Her heterophile antibody titer was negative; the icterus index was 13.8 units (normal being 4 to 6 for the method used); her hemoglobin level was 7.5 gms., hematocrit reading was 21%, white blood count was 13,000 with 72% polymorphs, 22% lymphocytes, 3% monocytes and 3% eosinophiles. Prothrombin time was 105% of standard. Occult blood was found in her stool. Other diagnostic procedures including chest x-ray and gastrointestinal series were normal.

The patient was treated with bed rest for three days while confirming laboratory tests, observations and examinations were made. Her icterus index rose to 32.5 on Nov. 14. The patient's temperature remained "low grade" being 99.2-99.4 orally at the highest points. After a period of complete bed rest and high carbohydrate diet, the diagnosis was confirmed by the internist, a second consultant, and this clinician. At no time in her illness did she receive chemotherapeutic agents.

Dramatic Improvement

The administration of Viron-1 was initiated and she received six intravenous 10 cc. injections during the remainder of her hospital stay. Following the second injection of Viron-1 the patient was amazed with her progress and remarked that she had lost the feeling of "being sick." She wanted to go home within 24 hours after Viron-1 injections were initiated, but hospitalization was continued. She was dismissed on Nov. 20, 1959, markedly improved in subjective feeling and dramatically improved clinically.

The patient was seen in my office on Dec. 1, 1959 at which time her white count had dropped to 7,000 with 53% polymorphs, 37% lymphocytes, 3% monocytes and 4% eosinophiles. Hemoglobin level was 12.8 gms. and her icterus index had dropped to 8.0.

There is no question in the mind of this investigator that the intravenous administration of Viron-1 had a profound therapeutic effect upon this patient. She had obtained minimal benefit from complete bed rest and high carbohydrate diet before the administration of Viron-1. She outwardly

* Viron-1 was supplied by Lincoln Laboratories, Inc., Decatur, Ill.

exhibited, and freely discussed with the attending physicians, her feeling of well-being following the administration of intravenous Viron-1. An accurate diagnosis of the exact type of hepatitis was impossible. It was assumed to be viral in nature; however, it may well have been a toxic condition. Other than the academics involved, the exact etiology is relative. The important factor to consider is that she responded to Viron-1 in a most satisfactory manner and one cannot but assume that the medication exerted a profound effect upon her progress.

Past experience with hepatitis of various etiologies has given this observer the impression that recovery from hepatitis, regardless of etiology, is extremely slow and painstaking. The rapid and complete response of this patient to Viron-1 has not been observed following classic and accepted therapeutic measures for treating hepatitis. It is difficult to comprehend a set of circumstances that would coincidentally explain the marked and rapid improvement in a patient as sick as this girl. It was certainly the most dramatic recovery from hepatitis that I have ever observed.

Infectious Mononucleosis

A while female, age 36, complained of generalized aching, exhaustion, anorexia and malaise. Her physical condition prior to these symptoms had been normal. Fever, remittent in type, accompanied the symptomatic complaints. A complete blood count revealed large vacuolated lymphocytes. A positive heterophile antibody titer of 1:226 was recorded. A diagnosis of acute infectious mononucleosis was made and intravenous Viron-1 therapy was initiated. Clinical and subjective response to three consecutive daily 10 cc. injections was excellent. Symptoms remitted in one week following beginning of therapy. The overall morbidity was reduced beyond expectation for the diagnosed condition. The medication was well tolerated and no adverse side effects were noted. The rapidity of patient response to Viron-1 was dramatic since full recovery from infectious mononucleosis rarely takes place in less than two to three weeks in my experience.

Virus Pneumonia

A 60-year-old male physician presented himself with a history of excellent health except for his present illness. His symptoms were exhaustion, cough, low grade fever, anorexia, generalized aching and profuse sweating upon exertion. Viral pneumonia—patchy type—of the right upper lobe was found and confirmed by x-ray findings. Treatment consisted of 10 cc. intravenous Viron-1 for three days, bed rest, and ASA Compound. The response was excellent—strength returned on the fourth day and on the fifth day the physician returned to work. The I. V. Viron-1 was well tolerated and no untoward side effects were observed. Viron certainly shortened the expected morbidity for a case of this nature.

Acute Viral Type Pneumonia

A female, age 47, was in excellent general physical condition with exception of chronic bronchiectasis. When first seen for her present illness this woman was completely debilitated. She was confined to her bed and complained of exhaustion, anorexia and generalized chest pain. Temperature elevation ranged from minimal to normal. A diagnosis was made of acute viral type pneumonia with secondary bacterial involvement of sinus and bronchial tree. She was given intravenous Viron-1, 10 cc. injections, on Oct. 26, 27 and 30 and Nov. 3, 6, 9, 1959. No other medication was utilized. Patient felt better after the second injection of Viron-1 and insisted on continued therapy. Her exhaustion syndrome continued to show remarkable improvement. Progress was continuous and the administration of Viron-1 markedly reduced morbidity as compared to her previous recurrent pneumonias. She tolerated the injections well and no adverse side effects were observed.

Viral Pneumonia and Bronchitis

A male, age 41, was in good physical condition except for the present illness and recurring pain from a herniated lumbosacral disk. He complained of headache, generalized muscular aching and exhaustion. His temperature was 100°-100.4° orally. The diagnosis was acute viral pneumonia and

bronchitis, following acute sinusitis. Injections of intravenous Viron-1, 10 cc., were given on July 14, 15, 16, 1959. The patient was seen for follow-up examination on July 23 and was symptom free. He had experienced marked relief both from sinusitis and viral pneumonia symptoms and had returned to work on fifth day following therapy without my permission. The morbidity period in this case was definitely shortened beyond expectation. Viron-1 was well tolerated by the patient and no side effects were observed.

Generalized Viremia

This male, age 72, was in fair general physical condition. Patient complained of "feeling bad", hoarseness, exhaustion and depression following "influenza." His temperature was normal, but he had a persistent cough. I made a diagnosis of generalized viremia with bronchitis and right recurrent laryngeal neuritis. Viron-1 was given intravenously on Oct. 28, 30 and Nov. 6, 1959. He experienced a relief of symptoms and felt better. Marked improvement in symptoms of viremia were observed. The medication was of questionable benefit to the neuritis. Viron-1 was well tolerated—no untoward side effects were observed.

Summary

In these selected six cases of probable viral infections, Viron-1 promoted prompt patient response. In four of the above mentioned cases improvement was especially rapid and dramatic. The patients were of different groups and conditions treated were varied. Of significant interest is the shortened morbidity period observed when Viron-1 was given either singly or in conjunction with other therapy. No untoward side effects were observed.

Conclusion

In the experience of this investigator daily doses of 2000 mg. of ascorbic acid fortified with B-complex vitamins given intravenously provides a valuable adjunct in the routine management of a variety of acute viral infections. Further investigation is warranted to determine the complete range of viral diseases which can be treated beneficially with this therapeutic adjunct.

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117 W. Washington St.
Shelbyville, Indiana

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WILSON L DALTON, M.D.
Shelbyville

TREATMENT OF VIRAL DISEASES presents to the physician a perplexing and frequently unrewarding problem, particularly since some 50 different diseases of man are of viral etiology. To date no generally effective therapeutic measures have been devised for treating viral diseases, although some diseases caused by the largest of the known viruses appear to be affected by some chemotherapeutic agents. Therapy with specific antisera is useful as a preventive measure during the incubation period of some viral diseases, but is generally of little value once clinical manifestations of the infection have ensued.¹ Therefore, an effective therapeutic agent that would substantially reduce the morbidity of the majority of viremias would provide the physician with a most valuable adjunct to treatment.

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McCormick⁴ administered ascorbic acid intravenously or intramuscularly in massive repeated doses, 500 to 1000 mg. every four hours. He reported that this approach exhibited a potent chemotherapeutic-like action in acute infectious processes which compared favorably to that of the sulfonamides or antibiotics but with the advantage of complete freedom from toxic or allergic reactions. Baur and Staub⁵ reported highly satisfactory results were obtained with daily intravenous infusions of 10 gm. of ascorbic acid in 1000 cc. of isotonic saline solution administered for an average of five days to patients with infectious hepatitis. They have described the action of ascorbic acid as "virucidal." Calleja and Brooks⁶ reported that daily intravenous infusion of 5 gms. of ascorbic acid for 24 days resulted in remarkable improvement in a patient with acute hepatitis when other therapeutic measures had proved futile.

Reports from German literature show

that high doses of vitamin C are beneficial in epidemic hepatitis in children. These beneficial effects were clearly observed in 63 cases of epidemic hepatitis treated with high doses of vitamin C in doses of 10 gms. daily for an average of five days given either by rectal infusion or intravenously, or both.⁹

This investigator evaluated a product trademarked Viron-1* as an adjunct in the treatment of a series of cases involving diseases of probable viral etiology. Viron is a preparation for intravenous administration consisting of 2000 mg. of ascorbic acid per dose fortified with certain B-vitamins. I was primarily concerned with patient response to this mode of therapy since time of recovery was of major economic importance to these patients. It has been my past experience that the more intense the patient's symptoms the greater the morbidity and the longer the convalescent period.

The following case histories are representative of this therapeutic regime:

Infectious Hepatitis

A 20-year-old white female hospital medical technician was first seen for the present illness on Nov. 9, 1959. The illness dates back to the spring of 1959 when she began to feel progressively weaker, exhibited malaise, anorexia, slight nausea, when it was discovered that she had an icteric tinge in her serum. She was treated with bed rest for four days and the sub-clinical jaundice disappeared with a return of her icterus index to normal.

Later in November her symptoms of malaise were intensified, she began to lose weight, became progressively weaker, and presented herself for examination. It was decided that she had clinical jaundice of a minor degree; however, the liver was not palpable and her physical examination was essentially normal.

She was hospitalized on Nov. 11 and was seen in consultation by an internist who confirmed the diagnosis of hepatitis, etiology unknown. Her admission laboratory work revealed a urine which was essentially

negative, except for the presence of bile. Her heterophile antibody titer was negative; the icterus index was 13.8 units (normal being 4 to 6 for the method used); her hemoglobin level was 7.5 gms., hematocrit reading was 21%, white blood count was 13,000 with 72% polymorphs, 22% lymphocytes, 3% monocytes and 3% eosinophiles. Prothrombin time was 105%- of standard. Occult blood was found in her stool. Other diagnostic procedures including chest x-ray and gastrointestinal series were normal.

The patient was treated with bed rest for three days while confirming laboratory tests, observations and examinations were made. Her icterus index rose to 32.5 on Nov. 14. The patient's temperature remained "low grade" being 99.2-99.4 orally at the highest points. After a period of complete bed rest and high carbohydrate diet, the diagnosis was confirmed by the internist, a second consultant, and this clinician. At no time in her illness did she receive chemotherapeutic agents.

Dramatic Improvement

The administration of Viron-1 was initiated and she received six intravenous 10 cc. injections during the remainder of her hospital stay. Following the second injection of Viron-1 the patient was amazed with her progress and remarked that she had lost the feeling of "being sick." She wanted to go home within 24 hours after Viron-1. injections were initiated, but hospitalization was continued. She was dismissed on Nov. 20, 1959, markedly improved in subjective feeling and dramatically improved clinically.

The patient was seen in my office on Dec. 1, 1959 at which time her white count had dropped to 7,000 with 53 % polymorphs, 37% lymphocytes, 3% monocytes and 4% eosinophiles. Hemoglobin level was 12.8 gms. and her icterus index had dropped to 8.0.

There is no question in the mind of this investigator that the intravenous administration of Viron-1 had a profound therapeutic effect upon this patient. She had obtained minimal benefit from complete bed rest and high carbohydrate diet before the administration of Viron-1. She outwardly

* Viron-1 was supplied by Lincoln Laboratories, Inc., Decatur, 111.

exhibited, and freely discussed with the attending physicians, her feeling of well-being following the administration of intravenous Viron-1. An accurate diagnosis of the exact type of hepatitis was impossible. It was assumed to be viral in nature; however, it may well have been a toxic condition. Other than the academics involved, the exact etiology is relative. The important factor to consider is that she responded to Viron-1 in a most satisfactory manner and one cannot but assume that the medication exerted a profound effect upon her progress.

Past experience with hepatitis of various etiologies has given this observer the impression that recovery from hepatitis, regardless of etiology, is extremely slow and painstaking. The rapid and complete response of this patient to Viron-1 has not been observed following classic and accepted therapeutic measures for treating hepatitis. It is difficult to comprehend a set of circumstances that would coincidentally explain the marked and rapid improvement in a patient as sick as this girl. It was certainly the most dramatic recovery from hepatitis that I have ever observed.

Infectious Mononucleosis

A while female, age 36, complained of generalized aching, exhaustion, anorexia and malaise. Her physical condition prior to these symptoms had been normal. Fever, remittent in type, accompanied the symptomatic complaints. A complete blood count revealed large vacuolated lymphocytes. A positive heterophile antibody titer of 1:226 was recorded. A diagnosis of acute infectious mononucleosis was made and intravenous Viron-1 therapy was initiated. Clinical and subjective response to three consecutive daily 10 cc. injections was excellent. Symptoms remitted in one week following beginning of therapy. The overall morbidity was reduced beyond expectation for the diagnosed condition. The medication was well tolerated and no adverse side effects were noted. The rapidity of patient response to Viron-1 was dramatic since full recovery from infectious mononucleosis rarely takes place in less than two to three weeks in my experience.

Virus Pneumonia

A 60-year-old male physician presented himself with a history of excellent health except for his present illness. His symptoms were exhaustion, cough, low grade fever, anorexia, generalized aching and profuse sweating upon exertion. Viral pneumonia—patchy type—of the right upper lobe was found and confirmed by x-ray findings. Treatment consisted of 10 cc. intravenous Viron-1 for three days, bed rest, and ASA Compound. The response was excellent—strength returned on the fourth day and on the fifth day the physician returned to work. The I. V. Viron-1 was well tolerated and no untoward side effects were observed. Viron certainly shortened the expected morbidity for a case of this nature.

Acute Viral Type Pneumonia

A female, age 47, was in excellent general physical condition with exception of chronic bronchiectasis. When first seen for her present illness this woman was completely debilitated. She was confined to her bed and complained of exhaustion, anorexia and generalized chest pain. Temperature elevation ranged from minimal to normal. A diagnosis was made of acute viral type pneumonia with secondary bacterial involvement of sinus and bronchial tree. She was given intravenous Viron-1, 10 cc. injections, on Oct. 26, 27 and SO and Nov. 3, 6, 9, 1959. No other medication was utilized. Patient felt better after the second injection of Viron-1 and insisted on continued therapy. Her exhaustion syndrome continued to show remarkable improvement. Progress was continuous and the administration of Viron-1 markedly reduced morbidity as compared to her previous recurrent pneumonias. She tolerated the injections well and no adverse side effects were observed.

Viral Pneumonia and Bronchitis

A male, age 41, was in good physical condition except for the present illness and recurring pain from a herniated lumbosacral disk. He complained of headache, generalized muscular aching and exhaustion. His temperature was 100°-100.4° orally. The diagnosis was acute viral pneumonia and

bronchitis, following acute sinusitis. Injections of intravenous Viron-1, 10 cc., were given on July 14, 15, 16, 1959. The patient was seen for follow-up examination on July 23 and was symptom free. He had experienced marked relief both from sinusitis and viral pneumonia symptoms and had returned to work on fifth day following therapy without my permission. The morbidity period in this case was definitely shortened beyond expectation. Viron-1 was well tolerated by the patient and no side effects were observed.

Generalized Viremia

This male, age 72, was in fair general physical condition. Patient complained of "feeling bad", hoarseness, exhaustion and depression following "influenza." His temperature was normal, but he had a persistent cough. I made a diagnosis of generalized viremia with bronchitis and right recurrent laryngeal neuritis. Viron-1 was given intravenously on Oct. 28, 30 and Nov. 6, 1959. He experienced a relief of symptoms and felt better. Marked improvement in symptoms of viremia were observed. The medication was of questionable benefit to the neuritis. Viron-1 was well tolerated—no untoward side effects were observed.

Summary

In these selected six cases of probable viral infections, Viron-1 promoted prompt patient response. In four of the above mentioned cases improvement was especially rapid and dramatic. The patients were of different groups and conditions treated were varied. Of significant interest is the shortened morbidity period observed when Viron-1 was given either singly or in conjunction with other therapy. No untoward side effects were observed.

Conclusion

In the experience of this investigator daily doses of 2000 mg. of ascorbic acid fortified with B-complex vitamins given intravenously provides a valuable adjunct in the routine management of a variety of acute viral infections. Further investigation is warranted to determine the complete range of viral diseases which can be treated beneficially with this therapeutic adjunct.

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117 W. Washington St.
Shelbyville, Indiana

Virus Pneumonia and Its Treatment With Vitamin C

FRED R. KLENNER, M.D., Reidsville, North Carolina

VIRUS PNEUMONIA (primary atypical pneumonia, non-specific pneumonitis, epidemic non-bacterial pneumonia, disseminated focal pneumonia, viral pneumonia) has been accepted as an entity and has been under observation in this country and abroad for the past twelve years. No bacteriological studies have confirmed the etiology of this disease other than by negative findings. The sputum shows the usual flora of gram-positive and gram-negative organisms. In 1938, Reimann reported that a filterable infectious agent was recovered from the nasopharynx of one and from the blood of another out of a series of eight cases, but not sufficient evidence could be found to determine such as the causative factor. It must be closely allied to the virus causing influenza, because in the first twenty-four to thirty-six hours it is very commonly thought to be that type of infection. Horsfall and his co-workers at the Rockefeller Institute have cultured an organism, which they have designated *Streptococcus MG*, from a large percentage of their patients with primary atypical pneumonia. The exact role of this bacterium is not known, but it is seldom found except in persons ill of this disease. Since it is not present in all cases, it is not the primary cause, but only a characteristic secondary invader or associate. The disease also resembles psittacosis in many respects and since penicillin might be of value in such cases it is of great importance to establish the diagnosis quickly.

The onset of this type of virus infection is always gradual. Like all virus diseases there is a wide variation of the prodromal symptoms. There might be none; there might be the classical generalized malaise. This disease is highly contagious, and our observations over a five-year period point to a definite incubation period of from five to fourteen days. We have also noted that the longer the incubation period the milder the infection; the shorter the incubation period the more severe is the infection. This must be interpreted in the first instance as either a mildly virulent organism or a high degree of resistance or immunity on the part of the host and in the second instance as a very virulent organism or no immunity at all on the part of the host. In some instances, however, the patient will have a slight attack with apparent recovery due either to good resistance against a weak virus or good response to treatment only to be followed in seven to ten days by a return of symptoms in a more severe form and producing a

critically ill patient. This type of case cannot be classified as a fourteen-day incubation period, but rather it is one in which the virus was only attenuated or else there has been the factor of a second infection.

The chief complaint, however, will always be one of sudden onset, since the patient begins his concept of his illness from the time he first experienced waves of chilly sensations or a frank chill alternating with hot spells and associated with burning in the nose, a sore throat, hoarseness, a bad taste in his mouth, moderate vertigo, nausea and grade-two type frontal headache. This picture will then develop to the point where severe frontal headache is noted along with a feeling of weakness in the lower extremities so marked that the patient complains of a dragging sensation when moving about in bed. This weakness persists for some days after clearing of all symptoms and negative chest films. The patient can hardly support his body weight without the feeling of buckling at the knees. Added to the above might be substernal pain or generalized tightness in the chest with varying degrees of tracheo-bronchitis. The fever is usually found during this phase to be about 102° F. After pulmonary involvement of as much as 6 by 8 cm. areas have been reached the fever will be up to 103 and 104° F. in adults and up to 105° F. in infants and early childhood. Dry hacking cough is a most constant factor especially after the second day of illness. Occasionally this cough is paroxysmal, and if the invasion is severe enough it will in the final clearing stage of the disease be thick, tenacious, brownish-gray — even blood-streaked. This disease shows remarkable versatility in that it will vary its symptoms and signs to fit with that of a mild cold on one hand to a very serious medical complexity on the other. It suggests sometimes that more than one bacteriologic unit is involved. The pulse will be increased in a very definite ratio to the toxic effect of the virus. If the invasion is mild the pulse rate will be normal even though the fever may be recorded at 103° F. If, however, the invasion is severe, meaning that physical findings approximating those of a lobar pneumonia (with or without a definite complicating encephalitis or meningitis) are present, or with an accompanying pleurisy, then the pulse rate will be rapid and will follow the temperature curve. Sweating is common and it is usually very profuse. Cyanosis and dyspnea occurred only in those patients that had at least as much as a lobe of lung involvement and where the fever continued to climb to a 104° F. each night.

The physical findings are limited to the head and chest. There is marked rhinitis with swelling of the turbinates. The accessory nasal sinuses are involved; the frontals being the chief offenders. The tonsil bed is not remarkable but the lymphoid tissue on the posterior pharyngeal wall is thickened and edematous and scarlet in color. The vocal cords appear like those seen in any simple laryngitis. In the lungs diminished breath sounds with moist and dry rales (sometimes very coarse) are usually the only evidence of disease. When there are extensive areas of consolidation the usual dullness to percussion, tubular breathing and pectoriloquy are present.

The laboratory findings are of little importance. The white blood count and differential are nearly always within normal limits. A 6500 white count is typical regardless of the lung pathology. The sedimentation rate will be normal except in very acute cases, with cerebral symptoms. The sputum examination is valuable only in its negative findings.

Chemotherapy may be tried where x-ray facilities are not convenient or not obtainable. If sulfonamides and/or penicillin are given for twenty-four to thirty-six hours without response both should be discontinued and treatment for virus infection instituted. In our age it requires some measure of boldness to discontinue these important drugs so early especially with the patient still running a fever of from 102 to 104° F. In this case boldness counts.

There is no constant x-ray picture to be found in virus pneumonia, but some evidence of pneumonitis will nearly always be present regardless of the physical signs—even when the physical signs are absent. The chest film will show anything from extensive consolidation to a patchy and sometimes fleecy infiltration suggestive of tuberculosis. This patchy form will be scattered in all diameters of the lung fields. Plates taken daily or every second to third day will often show the pneumonic process clearing in some areas while new areas are developing at other points. The disease begins as an infiltrative process starting at the hilus, and then, by a peribronchial route gradually spreading to the interbronchial regions. Usually there will be an involvement of several segments of lung comprising several lobes. These isolated segments soon become confluent, giving the film a smoky appearance. This process may go on to involvement of an entire lobe and in many respects look like a lobar pneumonia. The marked difference lies in the fact that even when the density is massive a streaky background can always be seen; the shadow in virus pneumonia is never entirely solid. Resolution, either spontaneous or from some method of treatment, may give positive x-ray films days and even

weeks after there has been a complete clinical response.

The treatment of virus infections, including frank virus pneumonia, has been for the most part without specific recommendations. Oppenheimer in 56 cases employed x-rays in doses from 35r to 90r which he states relieved cough and shortened the course of the disease. Offutt employed 100r doses daily or every other day, depending on the severity and response, alternating front and back or alternating sides if both lungs were involved. None in his series of twelve cases received over four treatments. Both men report surprising uniformity in the disappearance of fever and symptoms after one or two exposures. No unfavorable reactions occurred in either series. Aminophyllin in doses of three grains every four hours has been given with varying results in the belief that it improved the circulation through the lung fields. We have employed the drug in smaller doses when there was evidence that the patient had a coexisting coronary impairment. Since this was given along with the drug of our choice, ascorbic acid, this paper cannot evaluate its merits. Multiple transfusions from multiple donors and blood from patients convalescing from virus pneumonia have also been used.

The purpose of this paper is to outline a new and different form of treatment for this type of virus infection which in 42 cases over a five-year period has given excellent results. The treatment has double merit due to the simplicity of its schedule. The remedy used was vitamin C (ascorbic acid) given in massive doses. Since it is common knowledge that there are definite individual variations in absorption of vitamin C from the intestinal tract and under certain pathological conditions still greater variations in the absorption factors the I. V. and I. M. routes were used. When a diagnosis of virus pneumonia was entertained the patient was given 1000 mg. vitamin C intravenously every six to twelve hours. If it was by chance that a diagnosis was established in the home the usual initial dose was 500 mg. given in the gluteal muscle. Subsequent injections were given I. V. because the injection was thus made painless and the response was faster. In infants and very small children, however, 500 mg. I. M. every six to twelve hours was the method of choice. From three to seven injections gave complete clinical and x-ray response in all of our cases. The series comprised types of cases from very slight consolidation to those resembling lobar pneumonia. Two cases were complicated by cerebral manifestations. Vitamin C was also given by mouth in one-third of this series but there was no outstanding difference in the response. The dosage was from 100 to 500 mg., depending on the age of the pa-

tient, and it was given every four to six hours. In almost every case the patient felt better within an hour after the first injection and noted a very definite change after two hours. Nausea was relieved by the first injection as was the headache. The heat regulating center showed a quick response and it was the rule to find a drop of 2° F. several hours after the first 1000 mg. Penicillin was given in conjunction with ascorbic acid in five cases. It was our observation that penicillin had some retarding effect on the action of vitamin C, since the response was not so rapid and in one case the results were not obtained until the penicillin was discontinued.

Supportive treatment was given by forcing fluids, particularly fruit juices, to tolerance. Soda-water was given to adults in the amount of four glasses in 24 hours, each glass containing one teaspoonful sodium bicarbonate. Infants and children were given this alkaline drink in proportion to age. The rationale of bicarbonate of soda is based on the findings of Hawley and others that the amount of vitamin C excreted in the urine may vary according to the acid:alkali content of the diet, a highly alkaline urine having lower amounts of vitamin C than a highly acid urine. Codeine sulfate and aspirin were given by mouth. In adults the dose was codeine 0.5 grain, aspirin 10 grains given every six hours. Infants and children according to age. Some few patients complained of severe chest pain and some others of a constricting sensation that they described as cutting off their breath. These symptoms were relieved by employing either Numotizine as a plaster or the old-fashioned mustard plaster. The mustard plaster was made up with cold water and was applied cold for a period of about 15 minutes. The proportions used were one part mustard and two parts flour. The amount of flour used in preparing the plaster for children was according to age but in no instance was the ratio greater than one to six. In childhood an expiratory grunt was taken as an index to use plasters. Oxygen inhalation was not employed even though cyanosis existed in twelve cases of the series; an additional injection of 500 mg. of vitamin C was given with almost spontaneous alleviation of the distressing condition. In two cases codeine sulfate was given in one grain amounts because of the weight of the patient. Diet was forced even though there was no desire to eat.

It is difficult to evaluate the role played by vitamin C against the virus organism. We have seen ascorbic acid give response in other types of virus infections but not sufficient evidence is on hand to state that it is a virus killer. It has been shown histologically that vitamin C regulates the intercellular substance of the capillary wall. In the human body its chief function is concerned

with the formation of colloidal intercellular substances. The intercellular substances which appear to be regulated by vitamin C are of mesenchymal origin—this means the collagen of all fibrous tissue structure, all non-epithelial cement substances including the intercellular substance of the capillary wall. Gothlin found increased capillary fragility in individuals with blood levels of 1 mg. of vitamin C per liter or less. It must be remembered too, however, that ascorbic acid has been reported to function as a respiratory catalyst, aiding cellular respiration by acting as a hydrogen transport.

Finally we consider the case of the liver in that the saturation of the blood plasma with vitamin C betters the detoxifying powers of this organ. It has been known that fever, toxemia and specific bacteria do act on the vitamin C concentration of the blood plasma with a lowering effect. Could it be that, by maintaining a high blood level of this vitamin, all body tissue is allowed to return to normal in spite of the existing fever and the presence of the specific organism, and that, acting as a respiratory catalyst, it enables the body to build up adequate resistance to the invader?

SUMMARY

Virus pneumonia is a true clinical entity. Although it gives symptoms similar to influenza in the early stage of illness the virus has not been identified. The onset is gradual and has an incubation period of five to fourteen days. The usual beginning is a hanging-on cold or generalized malaise. The chief symptoms, although not all are necessarily present each time, are chilly sensations or a single frank chill, followed with hot spells, burning in the nose, sore throat, hoarseness, bad taste in mouth, nausea, frontal headache, dry cough at first—later productive in the clearing phase of the disease—sweating, and this is usually profuse, normal pulse unless complicated with cerebral symptoms, pleurisy or a condition approximating lobar pneumonia when it will be rapid. Fever is from 100 to 104° F. The physical findings are inflammation of the turbinates and accessory nasal sinuses, hypertrophy of the lymphoid tissue on the posterior pharyngeal wall. Breath sounds are diminished and moist and dry rales are sometimes present. In extensive consolidation dullness to percussion, tubular breathing and pectoriloquy are found. The laboratory findings show the blood picture within normal limits; the sputum is negative. Sulfonamides and penicillin are good diagnostic aids since they have no effect on the disease. The x-ray findings can be anything from negative films through pneumonitis on to frank consolidation. Vitamin C in doses of 1000 mg. every six to twelve hours for three to seven injections has been specific in the experience of the author. X-ray in

VIRUS PNEUMONIA—From P. 38

doses from 35 to 100r daily, or every second to third day, for not more than four exposures, aminophyllin and transfusions from convalescing or multiple donors have some usefulness as adjuvants in some cases.

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Read by Title to the Tri-State Medical Association of the Carolinas and Virginia, meeting at Charleston, February 9th and 10th.

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The laboratory findings are of little importance. The white blood count and differential are nearly always within normal limits. A 6500 white count is typical regardless of the lung pathology. The sedimentation rate will be normal except in very acute cases, with cerebral symptoms. The sputum examination is valuable only in its negative findings.

Chemotherapy may be tried where x-ray facilities are not convenient or not obtainable. If sulfonamides and/or penicillin are given for twenty-four to thirty-six hours without response both should be discontinued and treatment for virus infection instituted. In our age it requires some measure of boldness to discontinue these important drugs so early especially with the patient still running a fever of from 102 to 104° F. In this case boldness counts.

There is no constant x-ray picture to be found in virus pneumonia, but some evidence of pneumonitis will nearly always be present regardless of the physical signs—even when the physical signs are absent. The chest film will show anything from extensive consolidation to a patchy and sometimes fleecy infiltration suggestive of tuberculosis. This patchy form will be scattered in all diameters of the lung fields. Plates taken daily or every second to third day will often show the pneumonic process clearing in some areas while new areas are developing at other points. The disease begins as an infiltrative process starting at the hilus, and then, by a peribronchial route gradually spreading to the interbronchial regions. Usually there will be an involvement of several segments of lung comprising several lobes. These isolated segments soon become confluent, giving the film a smoky appearance. This process may go on to involvement of an entire lobe and in many respects look like a lobar pneumonia. The marked difference lies in the fact that even when the density is massive a streaky background can always be seen; the shadow in virus pneumonia is never entirely solid. Resolution, either spontaneous or from some method of treatment, may give positive x-ray films days and even

weeks after there has been a complete clinical response.

The treatment of virus infections, including frank virus pneumonia, has been for the most part without specific recommendations. Oppenheimer in 56 cases employed x-rays in doses from 35r to 90r which he states relieved cough and shortened the course of the disease. Offutt employed 100r doses daily or every other day, depending on the severity and response, alternating front and back or alternating sides if both lungs were involved. None in his series of twelve cases received over four treatments. Both men report surprising uniformity in the disappearance of fever and symptoms after one or two exposures. No unfavorable reactions occurred in either series. Aminophyllin in doses of three grains every four hours has been given with varying results in the belief that it improved the circulation through the lung fields. We have employed the drug in smaller doses when there was evidence that the patient had a coexisting coronary impairment. Since this was given along with the drug of our choice, ascorbic acid, this paper cannot evaluate its merits. Multiple transfusions from multiple donors and blood from patients convalescing from virus pneumonia have also been used.

The purpose of this paper is to outline a new and different form of treatment for this type of virus infection which in 42 cases over a five-year period has given excellent results. The treatment has doable merit due to the simplicity of its schedule. The remedy used was vitamin C (ascorbic acid) given in massive doses. Since it is common knowledge that there are definite individual variations in absorption of vitamin C from the intestinal tract and under certain pathological conditions still greater variations in the absorption factors the I. V. and I. M. routes were used. When a diagnosis of virus pneumonia was entertained the patient was given 1000 mg. vitamin C intravenously every six to twelve hours. If it was by chance that a diagnosis was established in the home the usual initial dose was 500 mg. given in the gluteal muscle. Subsequent injections were given I. V. because the injection was thus made painless and the response was faster. In infants and very small children, however, 500 mg. I. M. every six to twelve hours was the method of choice. From three to seven injections gave complete clinical and x-ray response in all of our cases. The series comprised types of cases from very slight consolidation to those resembling lobar pneumonia. Two cases were complicated by cerebral manifestations. Vitamin C was also given by mouth in one-third of this series but there was no outstanding difference in the response. The dosage was from 100 to 500 mg., depending on the age of the pa-

tient, and it was given every four to six hours. In almost every case the patient felt better within an hour after the first injection and noted a very definite change after two hours. Nausea was relieved by the first injection as was the headache. The heat regulating center showed a quick response and it was the rule to find a drop of 2° F. several hours after the first 1000 mg. Penicillin was given in conjunction with ascorbic acid in five cases. It was our observation that penicillin had some retarding effect on the action of vitamin C, since the response was not so rapid and in one case the results were not obtained until the penicillin was discontinued.

Supportive treatment was given by forcing fluids, particularly fruit juices, to tolerance. Soda-water was given to adults in the amount of four glasses in 24 hours, each glass containing one teaspoonful sodium bicarbonate. Infants and children were given this alkaline drink in proportion to age. The rationale of bicarbonate of soda is based on the findings of Hawley and others that the amount of vitamin C excreted in the urine may vary according to the acid:alkali content of the diet, a highly alkaline urine having lower amounts of vitamin C than a highly acid urine. Codeine sulfate and aspirin were given by mouth. In adults the dose was codeine 0.5 grain, aspirin 10 grains given every six hours. Infants and children according to age. Some few patients complained of severe chest pain and some others of a constricting sensation that they described as cutting off their breath. These symptoms were relieved by employing either Numotizine as a plaster or the old-fashioned mustard plaster. The mustard plaster was made up with cold water and was applied cold for a period of about 15 minutes. The proportions used were one part mustard and two parts flour. The amount of flour used in preparing the plaster for children was according to age but in no instance was the ratio greater than one to six. In childhood an expiratory grunt was taken as an index to use plasters. Oxygen inhalation was not employed even though cyanosis existed in twelve cases of the series; an additional injection of 500 mg. of vitamin C was given with almost spontaneous alleviation of the distressing condition. In two cases codeine sulfate was given in one grain amounts because of the weight of the patient. Diet was forced even though there was no desire to eat.

It is difficult to evaluate the role played by vitamin C against the virus organism. We have seen ascorbic acid give response in other types of virus infections but not sufficient evidence is on hand to state that it is a virus killer. It has been shown histologically that vitamin C regulates the intercellular substance of the capillary wall. In the human body its chief function is concerned

with the formation of colloidal intercellular substances. The intercellular substances which appear to be regulated by vitamin C are of mesenchymal origin—this means the collagen of all fibrous tissue structure, all non-epithelial cement substances including the intercellular substance of the capillary wall. Gothlin found increased capillary fragility in individuals with blood levels of 1 mg. of vitamin C per liter or less. It must be remembered too, however, that ascorbic acid has been reported to function as a respiratory catalyst, aiding cellular respiration by acting as a hydrogen transport.

Finally we consider the case of the liver in that the saturation of the blood plasma with vitamin C betters the detoxifying powers of this organ. It has been known that fever, toxemia and specific bacteria do act on the vitamin C concentration of the blood plasma with a lowering effect. Could it be that, by maintaining a high blood level of this vitamin, all body tissue is allowed to return to normal in spite of the existing fever and the presence of the specific organism, and that, acting as a respiratory catalyst, it enables the body to build up adequate resistance to the invader?

SUMMARY

Virus pneumonia is a true clinical entity. Although it gives symptoms similar to influenza in the early stage of illness the virus has not been identified. The onset is gradual and has an incubation period of five to fourteen days. The usual beginning is a hanging-on cold or generalized malaise. The chief symptoms, although not all are necessarily present each time, are chilly sensations or a single frank chill, followed with hot spells, burning in the nose, sore throat, hoarseness, bad taste in mouth, nausea, frontal headache, dry cough at first—later productive in the clearing phase of the disease—sweating, and this is usually profuse, normal pulse unless complicated with cerebral symptoms, pleurisy or a condition approximating lobar pneumonia when it will be rapid. Fever is from 100 to 104° F. The physical findings are inflammation of the turbinates and accessory nasal sinuses, hypertrophy of the lymphoid tissue on the posterior pharyngeal wall. Breath sounds are diminished and moist and dry rales are sometimes present. In extensive consolidation dullness to percussion, tubular breathing and pectoriloquy are found. The laboratory findings show the blood picture within normal limits; the sputum is negative. Sulfonamides and penicillin are good diagnostic aids since they have no effect on the disease. The x-ray findings can be anything from negative films through pneumonitis on to frank consolidation. Vitamin C in doses of 1000 mg. every six to twelve hours for three to seven injections has been specific in the experience of the author. X-ray in

To Page 46

VIRUS PNEUMONIA—From P. 38

doses from 35 to 100r daily, or every second to third day, for not more than four exposures, aminophyllin and transfusions from convalescing or multiple donors have some usefulness as adjuvants in some cases.

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In this 1949 article, Dr. Fred Klenner reports successfully treating polio, diphtheria, herpes zoster, herpes simplex, chicken pox, influenza, measles, mumps, and viral pneumonia with injections of large doses of vitamin C. "The results," he says, "which we have reported in virus diseases using vitamin C as the antibiotic may seem fantastic. These results, however, are no different from the results we see when administering the sulfa, or the mold-derived drugs against many other kinds of infections."—*R.D.M.*

The Treatment of Poliomyelitis and Other Virus Diseases with Vitamin C

Fred R. Klenner, M.D., Reidsville, North Carolina

Journal of Southern Medicine and Surgery, July 1949, Vol. 111, No. 7, pp. 209–214

In a previous report dealing with the antagonistic properties of ascorbic acid to the virus of atypical pneumonia, mention was made of the fact that other types of virus infections had responded favorably to vitamin C. This paper is to present these findings as well as the results of subsequent studies on the virus of poliomyelitis, the viruses causing measles, mumps, chickenpox, herpes zoster, herpes simplex and influenza. Further studies with the virus of atypical pneumonia will also be discussed.

These observations of the action of ascorbic acid on virus diseases were made independently of any knowledge of previous studies using vitamin C on virus pathology, except for the negative report of Sabin after treating Rhesus monkeys experimentally infected with the poliomyelitis virus. A review of the literature in preparation of this paper, however, presented an almost unbelievable record of such studies. The years of labor in animal experimentations; the cost in human effort and in "grants," and the volumes written, make it difficult to understand how so many investigators could have failed in comprehending the one thing that would have given positive results a decade ago. This one thing was the size of the dose of vitamin C employed and the frequency of its administration. In all fairness it must be said that Jungeblut noted on several occasions that he attributed his failure of results to the possibility that the strength of his injectable "C" was inadequate. It was he who unequivocally said that "vitamin C can truthfully be designated as the antitoxic and antiviral vitamin."

In developing this paper it was felt that, since all virus infections were more or less akin, only one of this family would be considered in detail. Poliomyelitis, because of its prevalence and the seriousness of the problem it presents, was chosen as the disease to be so treated.

Poliomyelitis is in most instances an acute febrile disease of sudden onset, with symptoms of a systemic infection which either abruptly abort or develop to hyperesthesia, asymmetry of reflexes and flaccid paralysis or palsies of muscle groups. It affects

individuals of all ages, but mainly children, as do more common childhood diseases to which class it most likely belongs. Only slight contact between the carrier of the virus and the susceptible person suffices in some cases for the transfer of the causative organism. In this respect and also in that the virus can be demonstrated in the nasal washings as early as six days before onset of symptoms, poliomyelitis resembles measles. We never have an epidemic of poliomyelitis preceding an epidemic of measles; the opposite is frequently true. This grouping of the virus organisms is too often repeated not to carry some significance. For example, atypical pneumonia and influenza are caused by closely allied viruses; so are chickenpox, herpes zoster and herpes simplex; so are measles, mumps and poliomyelitis. The incubation period depends on the mode of entry. In experimental animals, Fraser and others showed that the average was 6.6 days with intracerebral inoculation and ten days when the intravenous route was used. Howitt mentions that the virus reaches the nervous system sooner after intranasal than after intravenous instillations. Transmission (Brodie, 1934) is by means of droplets from the mucous membrane of the upper respiratory tract. Infection by means of raw milk, human feces and house flies is highly improbable.

The research of Flexner, Clark and Amoss in 1914 proved that poliomyelitis is a disease of the entire nervous system, that the sensory ganglia are the seats of early and profound histological changes. The disease is significant mainly for the paralysis produced through injury to the motor neurons of the spinal cord and brain. This is caused by a special affinity of the virus for a certain type of nerve tissue. Experiments show the cerebral cortex to be the most unsatisfactory site for growth, that large amounts of the virus placed in this area are apt to disappear in a short time. Observations in monkeys and in man show that the anterior horn cells, particularly those of the lumbar cord, are the most favorable sites for proliferation of the virus.

In all clinically ill patients the virus eventually travels in the course of its invasion by several channels. The virus can make a direct assault through the olfactory bulb, to the brain, medulla and spinal cord. The virus can enter the blood stream directly or through the lymph channels. Following damage to the natural protective barrier, the choroid plexus, it can make its way to the central nervous system, or it can be excreted back onto the nasal mucous membrane where it will pick up the direct route of the olfactory bulb.

Clark, Turner and Reynolds (1926, 1927, 1929) concluded that the virus chiefly travels by the direct route to the brain. Lennette and Hudson (1935) confirmed this theory and reported their studies indicating that human infection is chiefly through the nasopharynx. Brodi and others showed that by section of the olfactory tracts in monkeys infection by the direct route was prevented. It is of more than mere academic interest that while the nasal mucosa of the monkey contains branches of the 5th and 7th cranial nerves and that in addition, since the virus can readily gravitate from the nasopharynx to the tonsil bed with its nerve supply, if the *olfactory tracts* are cut no infection will occur. The most likely explanation is that the olfactory is non-medullated. the neurones lie in the nasal mucosa and are thus exposed to the virus. The sciatic nerve (Brodi) will transport the virus only when it has been injured, suggesting that lack of myelin may render the healthy olfactory nerve vulnerable to the virus.

The most important of the secondary routes of infection is by the excretion of the virus from the blood stream onto the nasal mucosa. Lennette and Hudson (1934, 1935) demonstrated in monkeys that by sectioning the olfactory tracts and then inoculating by the intravenous route with the virus of poliomyelitis, they could prevent infection.

This would fit in with the work of Jungeblut and others that the spread of the virus through the central nervous system is along nerve tracts, rather than by means of the cerebrospinal fluid, the infection to become manifest when the first cell group is reached, and by relays of fibers, reaches the midbrain. Here numerous fiber-paths run in all directions and the virus is carried by both motor and sensory axons, causing disease at many levels of the brain and cord.

Since there is always a period of septicemia in the first few days of poliomyelitis, it might be that this is the all-important route and that the virus is grown on a living tissue, the blood, and then is deposited out on the surface of the olfactory bulb. From this we conclude that the time to destroy the virus is during this incubation period which varies more with virulence and power of multiplication than with size of initial dose.

The second flanking maneuver of importance is through the choroid plexus. It is the function of the choroid plexus and the pial lymphatic vessels to exclude the virus present in the blood from the nervous system. Once these protective structures are injured, however, the exclusion ceases and infection can follow readily. Changes in the structure or function of the meningeal choroid plexus complex, too slight to be detected in the cerebrospinal fluid or as morphological alterations, materially diminish its protective power. Flexner and Amoss injected large doses of the virus intravenously, then tested the cerebrospinal fluid and found no virus after the first 48 hours; virus in small amounts at the end of 72 hours; after 96 hours evidence of free access to this system. The virus was still present 19 days later when paralysis was beginning.

Poliomyelitis in man is always more severe if exercise is taken at time of the infection. Here one must consider the factor of filtration of the virus through the choroid plexus as being increased due to the elevation of the vascular bed pressure. Also, that, by the acceleration of the blood flow caused by greater oxygen demand in physical effort, a marked increase in the percentage of the virus deposited on the nasal mucosa would result.

We must agree with Fairbrother and Hurst that too little consideration has been given to the pathology of the nervous system and in particular to the drainage of the tissue fluids. These men confirmed the earlier work of Schröder, who stressed that the normal flow of these fluids is along the perivascular spaces from the center of the cord outward, and that any inflammatory exudate occupying these spaces must be swept into the pial meshes; further that meningeal infiltration may seem nothing more than a drainage of cells from the interior of the cord. Fairbrother and Hurst found that meningeal infiltration does not occur in monkeys until the perivascular infiltration beginning in the deeper vessels reaches the surface.

The presence of the filtrable microorganism or virus of poliomyelitis upon the mucous membrane of the nose and throat does not necessarily lead to infection. It may give rise to a class of healthy carriers who are themselves immune. Amoss and Taylor found a secretion of the mucous membrane capable of neutralizing or inactivating the virus, this property absent altogether from the secretions of some persons, in those of

others present at time and not at another. It is probable that in actively immune animals the passage of the neutralizing substance from the blood into the cerebrospinal fluid would continue as long as the inflammation present in the meninges rendered the structures easily permeable to the protein constituents of the blood. This secretion *X* could not have the properties of a true antibody. The virus of poliomyelitis is intracellular from the time it invades the terminal cells of the olfactory system until the end of the disease, except when crossing the synaptic junctions between cells. This explains why the virus cannot be neutralized by antibodies in the serum. Further protection is afforded the virus by the functional barrier between the circulating blood and the central nervous system.

Since immunization against poliomyelitis comparable to that against other bacterial diseases is still a matter of the future, it suggested itself that some antibiotic could be found that would destroy this scourge while in the phase of blood-stream invasion. Sabin's negative report on the value of ascorbic acid on the poliomyelitis virus stopped Jungeblut's work, but we were cognizant of its dramatic effect on the virus causing atypical pneumonia, and so kept up hope. These results were so consistently positive that we did not hesitate to try its effectiveness against all types of virus infections. The frequent administration of massive doses of vitamin C was so encouraging in the early days of the 1948 epidemic of poliomyelitis that a review of the literature was begun. Heaslip, in the *Australian Journal of Experimental Biology & Medicine* reported a mean urinary output of vitamin C under a load test of 19.9 per cent in 60 poliomyelitis cases, as contrasted with a mean figure of 44.3 per cent in 45 healthy contacts. This was suggestive of some relationship between the degree of vitamin C saturation and the infectious and noninfectious state. He was also able to show a correlation between the severity of the attack and the level of urinary excretion of the vitamin. This would indicate that a deficiency of vitamin C in the diet predisposed to infection and to severity of attack. Sabin reported no appreciable difference in infectivity of poliomyelitis in monkeys with much or no vitamin C in the diet. Many others, however, have reported that a "deficient vitamin C nutrition increases susceptibility to infection," and many others that animals dying from the effects of the poliomyelitis virus show a reduction of vitamin C in the tissues. Heaslip found a definite relationship between the severity of the infection and the level of vitamin C nutrition. It is consistent with accepted physiological action of vitamin C to expect an anti-edema effect in any given affected area. It is worthy of note that bacterial toxins can cause losses of from 50 to 85 per cent of the vitamin C normally contained in the adrenals. Jungeblut's investigations seemed to justify the conclusion that vitamin C was the "antibiotic" that would destroy the virus organism. He stated that the prophylactic and therapeutic administration of synthetic or natural vitamin C had given evidence of having distinct therapeutic properties in experimental poliomyelitis, and that the proper injection dose was directly proportional to the speed of the infection and the stage at which the process had arrived. Jungeblut stated in 1937 that the parenteral administration of natural vitamin C during the incubation period of poliomyelitis in monkeys is always followed by a distinct change in the severity of the disease; that after the fifth day of the disease distinctly larger doses are required. He realized, at that early date, that for a fast progressing infection such as results from the R. M. V. strain, very

large doses—400 mg. crystalline C maximum in a 24-hour period—of vitamin C would be required; for the Aycock virus with its slower infection potential small amounts of the vitamin would suffice. Even with almost infinitesimal amounts—100 mg. ascorbic acid for each 24-hour period—he was able to demonstrate that the nonparalytic survivors in one series was six times as great as in the controls. In our work we shall speak of six, ten and 20 thousand mg. in a similar time period.

Harde et al. reported that diphtheria toxin is inactivated by vitamin C in vitro and to a lesser extent in vivo. I have confirmed this finding, indeed extended it. Diphtheria can be cured in man by the administration of massive frequent doses of hexuronic acid (vitamin C) given intravenously and/or intramuscularly. To the synthetic drug, by mouth, there is little response, even when 1000 to 2000 mg. is used every two hours. This cure in diphtheria is brought about in half the time required to remove the membrane and give negative smears by antitoxin. This membrane is removed by lysis when "C" is given, rather than by sloughing as results with the use of the antitoxin. An advantage of this form of therapy is that the danger of serum reaction is eliminated. The only disadvantage of the ascorbic acid therapy is the inconvenience of the multiple injections. This concept of the action of vitamin C against certain toxins has led to treating other diseases producing exotoxins. For years it has been our knowledge that vitamin C in 500 to 1000 mg. doses injected I. M. would cure bacillary dysentery of the Shiga type. Children having 10 to 15 bloody stools per day have cleared in 48 hours under this schedule while at the same time reverting to normal feedings. This dual action of vitamin C against certain toxins and the virus organism becomes more intelligible with the work of Kligler, Warburg and others who believed that the detoxication effected by hexuronic acid is brought about by a direct combination of the vitamin with the toxin or virus, this followed by oxidation of the new compound which destroys both the virus or toxin and the vitamin. Borsook et al. decided that the main chemical action of ascorbic acid is as a powerful reducing agent, and the virus causing poliomyelitis is known to be susceptible to the oxidizing action of various agents. It is in point here to remark that vitamin C is an integral part of the oxidation-reduction system of the body, thus playing a definite part in natural resistance.

In the poliomyelitis epidemic in North Carolina in 1948, 60 cases of this disease came under our care. These patients presented all or almost all of these signs and symptoms: Fever of 101 to 104.6°, headache, pain at the back of the eyes, conjunctivitis, scarlet throat; pain between the shoulders, the back of the neck, one or more extremity, the lumbar back; nausea, vomiting and constipation. In 15 of these cases the diagnosis was confirmed by lumbar puncture; the cell count ranging from 33 to 125. Eight had been in contact with a proven case; two of this group received spinal taps. Examination of the spinal fluid was not carried out in others for the reasons: (1) Flexner and Amoss had warned that "simple lumbar puncture attended with even very slight hemorrhage opens the way for the passage of the virus from the blood into the central nervous system and thus promotes infection." (2) A patient presenting all or almost all of the above signs and symptoms during an epidemic of poliomyelitis must be considered infected with this virus. (3) Routine lumbar puncture would have made it obligatory to report each case as diagnosed to the health authorities. This would have deprived myself of

valuable clinical material and the patients of most valuable therapy, since they would have been removed to a receiving center in a nearby town.

The treatment employed was vitamin C in massive doses. It was given like any other antibiotic every two to four hours. The initial dose was 1000 to 2000 mg., depending on age. Children up to four years received the injections intramuscularly. Since laboratory facilities for whole blood and urine determinations of the concentration of vitamin C were not available, the temperature curve was adopted as the guide for additional medication. The rectal temperature was recorded every two hours. No temperature response after the second hour was taken to indicate the second 1000 or 2000 mg. If there was a drop in fever after two hours, two more hours was allowed before the second dose. This schedule was followed for 24 hours. After this time the fever was consistently down, so the drug was given 1000 to 2000 mg. every six hours for the next 48 hours. All patients were clinically well after 72 hours. After three patients had a relapse the drug was continued for at least 48 hours longer—1000 to 2000 mg. every eight to 12 hours. Where spinal taps were performed, it was the rule to find a reversion of the fluid to normal after the second day of treatment.

For patients treated in the home the dose schedule was 2000 mg. by needle every six hours, supplemented by 1000 to 2000 mg. every two hours by mouth. The tablet was crushed and dissolved in fruit juice. All of the natural "C" in fruit juice is taken up by the body; this made us expect catalytic action from this medium. Rutin, 20 mg., was used with vitamin C by mouth in a few cases, instead of the fruit juice. Hawley and others have shown that vitamin C taken by mouth will show its peak of excretion in the urine in from four to six hours. Intravenous administration produces this peak in from one to three hours. By this route, however, the concentration in the blood is raised so suddenly that a transitory overflow into the urine results before the tissues are saturated. Some authorities suggest that the subcutaneous method is the most conservative in terms of vitamin C loss, but this factor is overwhelmingly neutralized by the factor of pain inflicted.

Two patients in this series of 60 regurgitated fluid through the nose. This was interpreted as representing the dangerous bulbar type. For a patient in this category postural drainage, oxygen administration, in some cases tracheotomy, needs to be instituted, until the vitamin C has had sufficient time to work—in our experience 36 hours. Failure to recognize this factor might sacrifice the chance of recovery. With these precautions taken, every patient of this series recovered uneventfully within three to five days.

In the treatment of other types of virus infections the same "fluid" dose schedule was adopted. In herpes zoster 2000 to 3000 mg. of vitamin C was given every 12 hours, this supplemented by 1000 mg. in fruit juice by mouth every two hours. Eight cases were treated in this series, all of adults. Seven experienced cessation of pain within two hours of the first injection and remained so without the use of any other analgesic medication. Seven of these cases showed drying of the vesicles within 24 hours and were clear of lesions within 72 hours. They received from five to seven injections. One patient, a diabetic, stated that she was always conscious of an uncomfortable feeling, but that it was not an actual pain. Although nine-tenths of the vesicles cleared in the usual 72-hour period, she was given 14 injections, the last seven of only 1000 mg. This extra therapy

was given because of a small ulceration, an inch in diameter, secondarily infected by rupture of the vesicles by a corset stave prior to the first visit. Vitamin C apparently had no effect on this lesion, which was healed in two weeks under compound tincture of benzoin locally and penicillin and sulfadiazine by mouth. (The patient objected to taking penicillin by needle.) One of the patients, a man of 65, came to the office doubled up with abdominal pain and with a history of having taken opiates for the preceding 36 hours. He gave the impression of having an acute surgical condition. A massive array of vesicles extended from the dorsal nerve roots to the umbilicus, a hand's breadth wide. He was given 3000 mg. of vitamin C intravenously and directed to return to the office in four to five hours. It was difficult to convince him that his abdominal pain was the result of his having "shingles." He returned in four hours completely free of pain. He was given an additional 2000 mg. of vitamin C, and following the schedule given above he recovered completely in three days.

In herpes simplex it is important to continue the treatment for at least 72 hours. We have seen "fever blisters" that appeared healed after two injections recur when therapy was discontinued after 24 hours. Vitamin C in a strength of 1000 mg. per 10 c.c. of buffered solution gave no response when applied locally. This was true no matter how often the applications were made. In several cases 10 mg. of riboflavin by mouth t.i.d. in conjunction with the vitamin C injections appeared to cause faster healing.

Chickenpox gave equally good response, the vesicles responding in the same manner as did those of herpes. These vesicles were crusted after the first 24 hours, and the patient well in three to four days. We interpreted this similarity of response in these three diseases to suggest that the viruses responsible were closely related to one another.

Many cases of influenza were treated with vitamin C. The size of the dose and the number of injections required were in direct proportion to the fever curve and to the duration of the illness. Forcing of fruit juice was always recommended, because of the frequency and ease of reinfection during certain periods of the year.

The response of virus encephalitis to ascorbic acid therapy was dramatic. Six cases of virus encephalitis were treated and cured with vitamin C injections. Two cases were associated with virus pneumonia; one followed chickenpox, one mumps, one measles and one a combination of measles and mumps. In the case that followed the measles-mumps complex, definite evidence was found to confirm the belief that massive, frequent injections are necessary in treating virus infections with vitamin C. This lad of eight years was first seen with a temperature of 104°. He was lethargic, very irritable when molested. His mother said he had gradually developed his present clinical picture over the preceding four or five days. His first symptom was anorexia which became complete 36 hours before his first examination. He next complained of a generalized headache, later he became stuporous. Although very athletic and active, he voluntarily took to his bed. He was given 2000 mg. of vitamin C intravenously and allowed to return home because there were no available hospital accommodations. His mother was asked to make an hourly memorandum of his conduct until his visit set for the following day. Seen 18 hours after the initial injection of vitamin C, the memorandum revealed a quick response to the antibiotic—after two hours he asked for food and ate a hearty supper, then played about the house as usual and then, for several hours, he appeared to have

completely recovered. Six hours following the initial injection, he began to revert to the condition of his first visit. When seen the second time temperature was 101.6° , he was sleepy but he would respond to questions. The rude irritability shown prior to the first injection was strikingly absent. A second injection of 2000 mg. vitamin C was given intravenously and 1000 mg. of "C" prescribed every two hours by mouth. The next day he was fever- and symptom-free. As a precautionary measure a third 2000 mg. was given with direction to continue the drug by mouth for at least 48 hours. He has remained well since. A lad of 12 years had generalized headache a week after having mumps, this followed by malaise, and in 12 hours a lethargic state and a fever of 105° . Admitted to hospital he was given 2000 mg. of vitamin C then, and 1000 mg. every two hours. Following the third injection he was sitting up in bed, laughing, talking, begging for food and completely without pain. He was discharged 24 hours following admission clinically well. Since relapses do occur if the drug is discontinued too soon, he was given 2000 mg. of vitamin C every 12 hours for two additional days.

The use of vitamin C in measles proved to be a medical curiosity. During an epidemic vitamin C was used prophylactically and all those who received as much as 1000 mg. every six hours, by vein or muscle, were protected from the virus. Given by mouth, 1000 mg. in fruit juice every two hours was not protective unless it was given around the clock. It was further found that 1000 mg. by mouth, four to six times each day, would modify the attack; with the appearance of Koplik's spots and fever, if the administration was increased to 12 doses each 24 hours, all signs and symptoms would disappear in 48 hours. If the drug was discontinued or reduced to three or four doses each 24 hours following the disappearance of Koplik's spots, within another 48-hour period the fever, the conjunctivitis and Koplik's spots would be back.

It was our privilege to observe this picture over and over in two little volunteer girls for 30 days. These "research helpers" were my own little daughters. The measles virus was eventually destroyed in this instance by continuing 12,000 mg. by mouth each 24 hours for four days. We interpreted this result to indicate that on withdrawing the drug with the cessations of signs and symptoms, a small quantity of the virus remained, which after another incubation period produced anew the first stage of measles; when the drug was continued beyond the clearing stage the virus was destroyed in toto. No case of post-measles bronchopneumonia was seen. The "measles-cough" of measles bronchitis was over with after three or four 1000 mg. injections of "C" at 6-hour intervals. This was true even when other medications well above the calculated dose range for cough had had no effect. Whenever a patient presented a mixed-virus infection, such as receding mumps and developing measles, it was found that double the calculated dose of vitamin C was necessary to obtain the usual results.

Of mumps, 33 cases were treated with ascorbic acid. When vitamin C was given at the peak of the infection the fever was gone within 24 hours, the pain within 36 hours, the swelling in 48 to 72 hours. Two cases were complicated with orchitis. A young man of 23 years developed bilateral orchitis one Friday morning, by seven o'clock that night he was in severe pain, had a fever of 105° and was nursing testicles the size of tennis balls. Vitamin C was started at this time—1000 mg. every two hours, intravenously. The pain began to subside following the first injection and ceased in 12 hours. There was no

fever after 36 hours. The patient was out of bed feeling his old self after 60 hours. He had received 25,000 mg. of "C" in this 60-hour period. An experiment involving three cousins: One, a boy of seven, had the old routine of bed rest, aspirin, and warm camphor oil applications and iodex to the swollen glands. This child had a rough time for a week. A second boy, aged 11, was allowed to develop mumps to the point of maximum swelling without any therapy, then given vitamin C, 1000 mg. intramuscularly, every two to four hours. This lad was entirely well in 48 hours. To the third patient, a girl of 9, vitamin C was given on the up curve when the swellings were 60 per cent of the expected, and the temperature recorded at 102.3°. The dose was 1000 mg. of vitamin C given intravenously every four hours. This child was well and remained so from the third day of treatment.

Further studies on virus pneumonia showed that the clinical response was better when vitamin C was given to these patients according to the dose schedule outlined for poliomyelitis. Where pneumonitis was demonstrated, the clearing of the chest film was parallel with the clinical recovery. In cases of consolidation of entire lobes the x-ray clearing lagged days behind the clinical response. In these cases 1000 mg. of "C" should be given every 12 hours for at least a week after the patient is apparently well. There was no change in the results as given in a previous paper; the patients were well in the third day of treatment.

In using vitamin C as an antibiotic no factor of toxicity need be considered. To confirm this observation 200 consecutive hospital patients were given ascorbic acid, 500 to 1000 mg. every four to six hours, for five to ten days. One volunteer received 100,000 mg. in a 12-day period. It must be remembered that 90 per cent of these patients did not have a virus infection to assist in destroying the vitamin. In no instance did examination of the blood or urine indicate any toxic reaction, and at no time were there any clinical manifestations of a reaction to the drug. When vitamin C was given by mouth one per cent of these patients vomited shortly after taking the drug. In half of these cases the vomiting was controlled by increasing the carbohydrate content of the mixture. This reaction was not interpreted as representing a toxic manifestation; rather it was thought to be due to a hypersensitive gastric mucosa. The dose was reduced from 1000 to 100 mg. in young children showing this complex; vomiting occurred as before. However, in these same patients administration of massive, frequent doses of vitamin C by needle effected a cure of the infection without causing vomiting.

From a review of the literature one can safely state that in all instances of experimental work with ascorbic acid on the virus organism the amount of virus used was beyond the range of the administered dose of this vitamin. No one would expect to relieve kidney colic with a five-grain aspirin tablet; by the same logic we cannot hope to destroy the virus organism with doses of vitamin C of 10 to 400 mg. The results which we have reported in virus diseases using vitamin C as the antibiotic may seem fantastic. These results, however, are no different from the results we see when administering the sulfa, or the mold-derived drugs against many other kinds of infections. In these latter instances we expect and usually get 48- to 72-hour cures; it is laying no claim to miracle-working then, when we say that many virus infections can be cleared within a similar time limit.

THE JOURNAL OF SOUTHERN MEDICINE AND SURGERY

306 NORTH TRYON STREET, CHARLOTTE, N. C.

The Journal assumes no responsibility for the authenticity of opinion or statement made by authors, or in communications submitted to this Journal for publication.



JAMES M. NORTINGTON, M.D., Editor

VOL. ~~CIII~~ 113

APRIL, 1951

No. 4

Massive Doses of Vitamin C and the Virus Diseases

F. R. KLENNER, M.D., Reidsville, North Carolina

IT has been reported that one of the mold-derived drugs, in addition to being a good antibiotic, is a super-vitamin. Conversely, we argue that vitamin C, besides being an essential vitamin, is a super-antibiotic. Vitamin C in vitro, if maintained at body temperature, inactivates certain toxins at an unbelievable rate. Five parts per thousand of vitamin C with toxins and appropriate controls, incubated at 37° C. for 48 hours showed when tested on mice the minimal lethal dose for the control tubes to be 1/16,000 c.c., while that from the mixture of vitamin C and toxin was only 1/1,000 of a c.c. (Klegler, Guggenheim, Warburg, 1938). In this study the loss of vitamin C in toxin broth and ordinary broth controls followed a constant pattern; the loss, however, was always greater in the toxin broth tube. The difference between the rate of disappearance of vitamin C in toxin and ordinary broth was more striking the greater the concentration of vitamin C. It is, therefore, reasonable to conclude that the degree of neutralization in a virus infection will be in proportion to the concentration of the vitamin and the length of time in which it is employed.

Since it has long been known that the virus organism resembles more the toxins and ferments than the common animate causes of disease, it would seem plausible that the detoxication effected

by vitamin C is produced by a direct combination of the vitamin with the toxin and/or virus, this followed by the oxidation of the new compound which destroys both the virus and/or toxin and the vitamin. This destruction of the virus by oxidation has been concurred in by many investigators. Since vitamin C is an integral part of the oxidation-reduction system of the body, its function in the role of an antibiotic becomes intelligible. To appreciate the antagonistic properties of vitamin C against the virus organism and the chemical ferments of exotoxin-producing microorganisms, one must forget its present academic status as a factor essential for life. A cow is valuable to the farmer not only for her ability to produce milk, but also as a source of organic fertilizer. Vitamin C, likewise, is important, not only as a detoxifying agent, as a catalyst aiding cellular respiration by acting as a hydrogen transport, as a catalyst in the assimilation of iron, and as a conservator of collagen fibers and bundles in tissues of mesenchymal origin; but, also, because of its function as a reducing agent or the precursor of such a substance. In this latter capacity it fulfills the requirements of an antibiotic. A striking phenomenon of vitamin C is the similarity of response, whether to correct pathologic processes due to a deficiency of this compound, acting as a vitamin; or to destroy the ferments of microorganisms, acting as an antibiotic.

Within a few hours after institution of adequate vitamin C therapy to correct an avitaminosis, his-

tological evidence of bone improvement is obtainable. Fibroblasts begin to form normal connective tissue and capillary buds are invading hemorrhagic areas (Youmans, 1941). Similar is its dramatic antibiotic action, the rule being clear evidence of clinical response within a few hours.

The purpose of this paper is to present clinical proof of such action for this vitamin.

Case 1 is one of premeasles in a ten-months-old baby. The term "premeasles" is adopted to express the syndrome of fever, redness of eyes and throat, catarrh, spasmodic bronchial cough and Koplik spots. Vitamin C, 65 mgm. per Kg. of body weight, was injected intramuscularly every four hours. The fever dropped from 105 to 97.6° F. within 12 hours. All symptoms showed marked clearing. This sudden drop in the fever was thought to be explainable on one of three grounds: 1) Common night drop. 2) Due to the antibiotic action of vitamin C. 3) Even if the vitamin C administration had been continued, possibly a moderate rise would have occurred in the late afternoon of the second day, granting a highly virulent organism and a poorly resisting host. To determine which of these deductions was valid, vitamin C was discontinued for a period of eight hours. At this point the rectal temperature was back up to 103.4. Vitamin C therapy was resumed and instead of the expected 8 P. M. climb, the temperature was down to 99.2 (R) eight hours later. The vitamin C injections were continued, the baby made an uneventful recovery and was discharged 60 hours following admission. No measles rash developed. Eighteen months have elapsed since this illness and the child has not had clinical measles. This is not due to the establishment of active immunity but to the lack of a second exposure.

Case 2 confirms the previous case. This case is that of a 22-months-old infant with symptoms identical with that just described. The same medication was followed; the same clinical course followed. Under parental pressure the child was discharged from the hospital within 36 hours, apparently well. Four days later the child's brother and sister broke out with measles, which ran the usual course, having received no specific therapy. Seven days later the 22-months child broke out with measles. This time vitamin C was not given. The case was judged as modified.

The response as observed in measles was characteristic for vitamin C *versus* virus infections. Two cases of virus pneumonia complicated by encephalitis were so unusual that case histories are given.

Case 3 is that of a colored woman, aged 28, with history (given by a relative) of chills and fever and chest and head cold for 14 days, severe headache for three days. In stupor when first seen, eye lids closed, a white foam at the mouth which

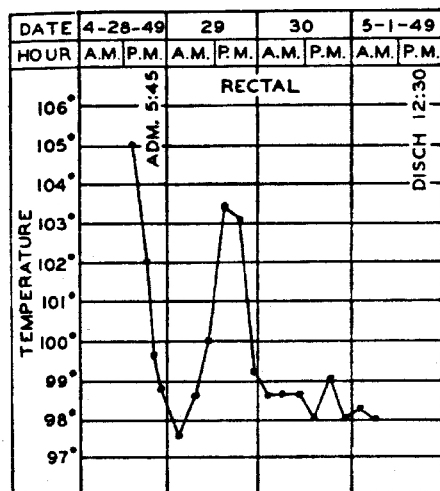
she periodically tried to spit out. Temperature by axilla 106.8. Dehydration was much in evidence, breath sounds diminished to absent, tactile fremitus increased over the entire right lung. The sulfa drugs, penicillin and streptomycin with supportive treatment had been exhausted. Four grams of vitamin C was given intravenously along with 1000 c.c. of 5 per cent dextrose in saline solution. Temperature dropped to 100 (Ax.) within 11 hours. Four hours later, vitamin C was resumed—every two to three hours, in dosage of 2 to 4 grams depending upon the response. After 72 hours the patient was awake, sitting up in bed and taking fluids freely by mouth. There was no fever at this time, nor for the remainder of the time in hospital. Vitamin C was continued for a period of two weeks; the frequency was cut to every 12 hours, two grams at a dose. An interesting complication was deafness; her speech gave a loud, monotonous, bell-sound effect. It was debated whether this was the result of the streptomycin or to the encephalitis. Prostigmin 1:2000, 1 c.c., and vitamin B₁, 200 mgm., were given IM twice daily. On the tenth day of treatment the hearing suddenly returned to normal. The x-ray picture of the right lung was one of almost complete consolidation. Although the patient was clinically well of her pneumonia after 72 hours, the x-ray picture was not completely clear until 90 days later.

This phenomenon of Nature clearing the debris after killing out the virus organism was observed in five other cases. The time required was in direct proportion to the degree of pulmonary involvement. There is nothing new about this procedure: Nature merely duplicating a stage in the metamorphosis of the frog in getting rid of its tadpole tail.

Case 4, that of a white baby 19 months old, bothered with a little cold for two weeks, not very sick until the last 24 hours, in which the baby had been "running a high fever that could not be broken with aspirin." Clonic convulsive seizures of the right arm and leg began 12 hours before admission. An undernourished infant, lying rigid in its mother's arms, skin cold to touch, color cadaver-like, eyes closed, grade -2 mucopurulent nasal discharge, throat red. The temperature was 103.8 (R). Breath and heart sounds practically inaudible. Areas of skin over the back presented an appearance similar to that seen in rigor mortis.

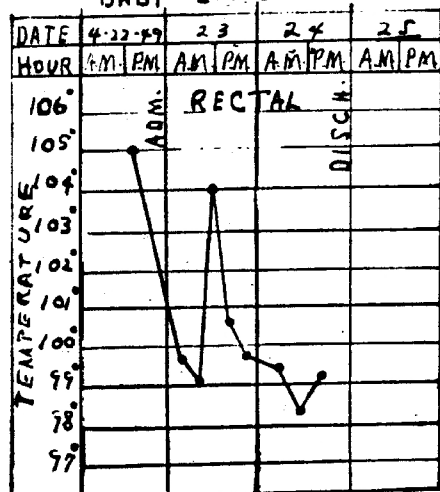
Vitamin C, 1000 mg., was given IM, repeated every four to six hours. At the first injection the baby did not move and the sensation was like that of sticking an orange. To give rapid external heat, mustard plasters were applied to the anterior and posterior chest in a mixture of one part mustard to three parts flour. A croup tent was set up, the vapor carrying compound tincture benzoin: 50

BABY D. S. (29753)



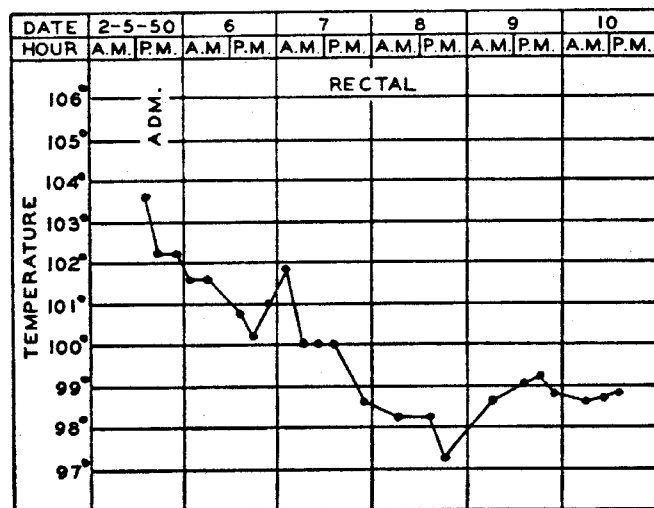
MEASLES

BABY J. S. O



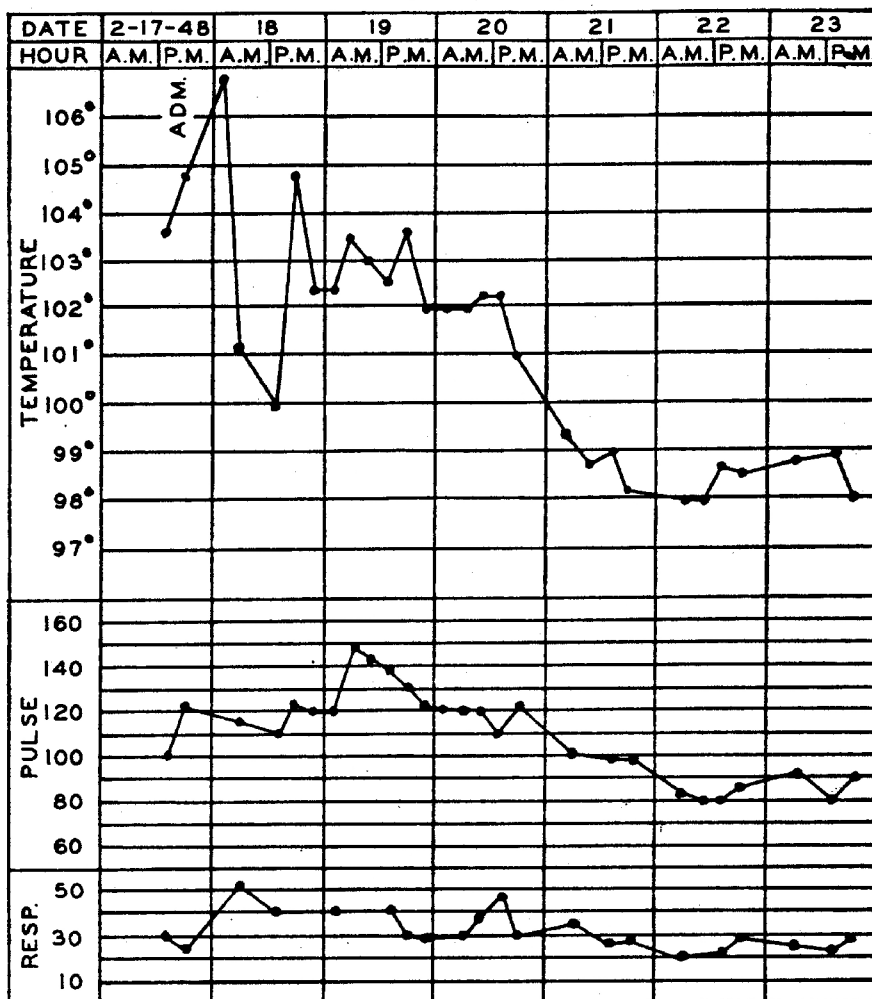
MEASLES

BABY W. M. (32219)



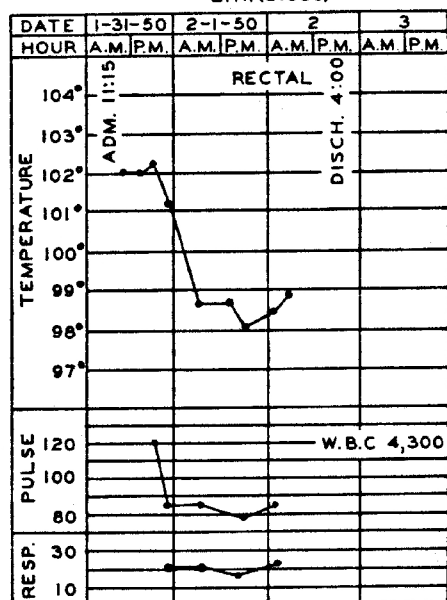
VIRUS ENCEPHALITIS-MENINGITIS

M. H. (26047)



VIRUS PNEUMONIA

L. R. (31680)



VIRUS INFECTION (PULMONARY)

c.c. of 5 per cent dextrose in saline was given under the skin in the scapular areas. Two hours after the first injection of vitamin C the baby drank 240 c.c. of orange juice, the first food of any type taken by the baby in 24 hours. This was repeated 1½ hours later. At this time there was total paralysis of the right arm and leg. Twelve hours after admission the baby moved its right leg and one hour later grasped a bottle of orange juice with both hands. From this point on the recovery was uneventful. Of secondary importance is the laboratory report of *Ascaris lumbricoides* ova and hemoglobin 55 per cent.

Cases 5 and 6 are of pulmonary virus infection, (a) in a boy of 14 years, and (b) in a man of 58 years. In the case of the boy the fever curve was of the type showing a fast response to heavy vitamin C injections. The WBC was 4,300, urine sugar ++. Twenty-six grams of vitamin C was given IV to this patient in a 44-hour period.

In the case of the man, Case 6, the fever decline was after a modified step-ladder fashion. In this instance the amount of vitamin C injected was less than half of the recommended dose. The WBC was 5,850, admission urine sugar +++. Thirty-one grams of vitamin C was injected intravenously over a period of 60 hours. It is to be noted that the same amount of vitamin C (2 grams every four hours) was given to the boy and to the man, disregarding the factor of body weight. Had the man received four or five grams every four hours, or two grams every two hours, his hospital course would probably have followed the same pattern as that of the boy. A point of great interest was that at subsequent examinations the urine was consistently negative for sugar. The course in these cases emphasizes the necessity of administering massive doses of vitamin C at frequent, regular intervals so as to maintain the proper level of this antibiotic in the tissues.

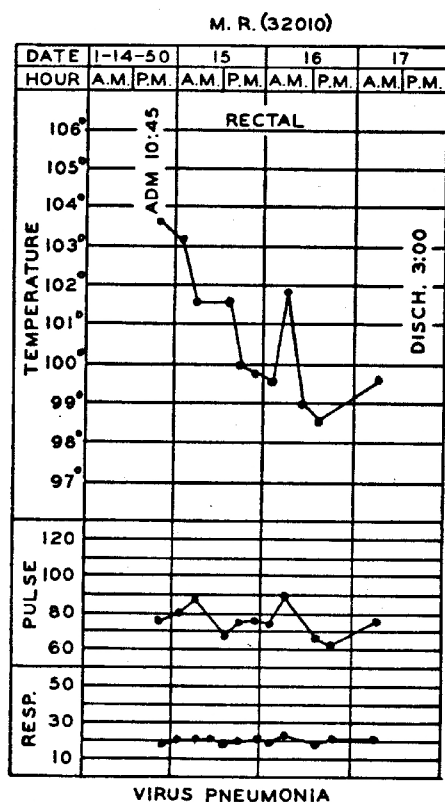
The amount of vitamin C for optimal effect will vary greatly with the individual. The type of the disease and the degree of toxemia are important guides in determining the dosage. Although the usual dose of vitamin C is calculated on the basis of 65 mgm. per Kg. of body weight, and given every two to four hours by needle, under certain conditions larger single injections can be used to good advantage. Vitamin C given to a child with measles, mumps or chickenpox will abort or modify the attack, depending upon the intensity of the treatment. If the activity of the pathogen is stopped, the development of active immunity will be interrupted. In handling these particular childhood diseases, when uncomplicated, the treatment should be aimed at modification of the infection as the plan of choice. To accomplish this end vitamin C should be increased to 250 mgm. per Kg. of

body weight, and the injection given intramuscularly. It will be necessary, at times, to repeat with half of this amount eight hours later. The vitamin was given in a concentration of 500 mg. per c.c. of solution. Pain was slight and lasted only a few minutes. Procaine, 0.5 to 2 per cent, instilled from a second syringe into the gluteal muscle through a placed needle just before giving the vitamin might solve this problem. The itch of measles and of chickenpox, the occasional vomiting of these illnesses, and the pain of mumps were fully controlled within one hour, when 250 mg./Kg. body weight was used. Instead of repeating waves of macules in chickenpox, and the usual seven to nine days required for crusting, following the heavy modifying injection no new eruptions appeared and crusting was present within six hours. Further clinical studies may prove that the routine use of the higher dose (250 mg./Kg. body wt.) replacing the usual (65 mg./Kg. body wt.) is indicated in all virus infections and the results produced may be even more dramatic.

The greatest value of vitamin C in virus infections does not rest with these lesser kinds of diseases, some of which, e.g. measles, can be modified or prevented by the proper use of immune globulin. The value above all others is its positive action against the virus causing poliomyelitis. A report of this usage was published in the official journal of this association in 1949. Many physicians refuse to employ vitamin C in the amounts suggested, simply because it is counter to their fixed ideas of what is reasonable; but it is not against their reason to try some new product being advertised by an alert drug firm. It is difficult for me to reconcile these two attitudes. On the other hand, many physicians who have been willing to try vitamin C against the virus of poliomyelitis have obtained the same striking results as we reported. Scores of letters from practitioners here in the United States and in Canada could be presented in evidence. In some instances doctors have cured their own children of poliomyelitis by giving vitamin C and in other cases doctors themselves have been cured.

In poliomyelitis vitamin C performs three important functions: 1) It destroys the virus; 2) acting as the dehydrator and diuretic of first choice, it removes the edema fluid from the brain and the cord; 3) it preserves the lining of the central canal and maintains more regular spacing and less crowding of the ependymal cells (Altman). The pressure within the bony vault of the central nervous system resulting from the inflammatory process excited by the virus, acts as a haemostat to cut off the blood supply to the anterior horn cells. This compression of their vessels denies to the horn cells the essentials for function, for life even.

It is of more than academic interest to review



sulfate as a compress gave prompt relief of the pain and swelling. In two of these cases fluctuation ensued and healing was effected by surgical drainage and the application of compresses. The impression in these two cases was that a vein had been opened by the needle. The exudate was dark and both the slide and culture studies were negative for bacteria. 3) Endothelial irritation in three cases. Acute pain radiated from the site of the injection to the shoulder. In each instance the concentration of the vitamin was one gram to each 5 c.c. solution and the amount given exceeded two grams. After slowing the rate of injection this reaction did not occur. 4) Venous thrombosis in one case. The concentration was 500 mg. per c.c. solution; the total dose 5 c.c. Compressing relieved the pain. The pathology was very similar to that following the use of 50 per cent dextrose solution. 5) Syncope—In maximum doses given IV a sensation of fainting and dyspnea occurred seven times. Five of these patients were over 55 years of age. The disagreeable symptoms were relieved by slowing the speed of the injections. 6) Rash—In three cases a pin-point dermatitis occurred, limited to the face and upper third of the torso, identical to that seen in infants taking orange juice. This did not necessitate discontinuance of therapy and cleared spontaneously several days after vitamin C was stopped.

Calcium, *in vivo*, duplicates the chemical behavior of vitamin C in many respects. Calcium gluconate and calcium lexulinate were used in conjunction with vitamin C therapy in a small series of pulmonary virus infections and in mild cases of influenza. There was a definite synergistic response. Patients with colds derived most benefit from this combined treatment. Because of its action on cardiac muscle, the use of calcium was limited to adults and the amount injected to two grams per day. One gram administered IV at moderate speed will so slow the heart as in many cases to produce syncope. If the concentration becomes great enough cardiac arrest in a tonically contracted state might result. It is, however, quite possible that, with the proper ionic balance of calcium and vitamin C in the same solution, larger amounts could be given without side effects. The massive dose schedule limits the usefulness of the calcium ion in virus diseases to that of an adjuvant only.

In all of the cases of virus infection reviewed in this study one laboratory finding stood out as of great significance. On admission to the hospital the first routine urine examination showed some degree of glycosuria. The pattern of the qualitative Benedict's reaction was constant enough to postulate that the higher the reading the more severe was the pathology. Repeat urine sugar studies following vitamin C therapy revealed complete clearing. This was true even though fruit juices were forced to tolerance. This finding confirmed the

knowledge that interference with the normal physiology of the adrenal glands, either by the toxins produced by microorganisms or by surgery, has a profound influence on metabolism, especially of the carbohydrates. Adrenalin in the blood stream causes hyperglycemia with resulting glycosuria. Adrenalin acts either by stimulation of the sympathetic nervous system or directly via the blood. This action of adrenalin is via the blood only, because the effect, as demonstrated in experimental animals, is still realized after destruction of the cord and sympathetic plexuses and degeneration of the peripheral post-ganglionic fibers (Evans, 1930). The glycosuria found in these cases was not due to a lowering of the threshold for sugar excretion by the kidney, paralleling a phloridzin diabetes, since the carbohydrate mechanism was associated with a hyperglycemia (Zuelzer, 1901, Metzger, 1902, Paton, 1903). Likewise there was no evidence of kidney damage. Albumin was reported negative and the microscopic examination showed no cells or casts. Apparently this is a condition of artificial diabetes mellitus, which would suggest the answer for the diabetic who loses ability to maintain sugar-insulin balance when embarrassed with an acute infection.

The story of a 7-year-old boy may have a lesson. He has been known to be diabetic since the age of four years. Any incident of infection in this lad produced an alarming interference of his sugar-insulin-diet equilibrium. Recently he contracted measles, and as the disease process developed toward its height the urine sugar curve swung sharply upward. From an occasional dose of 5 units regular insulin his requirement rose to 30 units regular insulin, three times each day, while still running a 3- or 4-plus Benedict's test. (Other forms of insulin proved by trial to be too dangerous.) At the peak of his infection vitamin C was started in a modifying dose of one gram every four hours. His general condition soon improved and in the course of several days he returned to his usual diet-insulin schedule and his usual urine sugar. In patients with diabetes, vitamin C should be discontinued just as soon as the temperature returns to normal. Prolonged use of vitamin C might prove undesirable due to its dehydrating and diuretic powers.

The pathologic process at work here is only compatible with abnormal amounts of adrenalin in the blood stream. It is not a response to an emotional stimulus to the adrenal medulla, since free adrenalin in the circulating blood has a transitory action, being so rapidly oxidized that none gets into the urine. This suggested that the regulator of the adrenalin mechanism had been removed, so that a constant supply of adrenalin would be present in the blood, making possible a concentration sufficiently high to cause constant vasoconstriction.

Ritzmann (1909) found that adrenalin affected carbohydrate metabolism only when this vasoconstriction phase existed. This finding was concurred in by Lusk (1914), who further concluded that this action on blood vessels caused asphyxia of the tissues which tended to increase the acidity of the blood and the tissues. This superimposed acidity further promotes the production of adrenalin hyperglycemia (Peters and Geyelin, 1917). McDannell and Underhill (1919), studying these phenomena in rabbits, found that slight hyperglycemia could be controlled by the administration of sodium carbonate.

The rationale of forcing fruit juices in the old treatment of colds was based on this theory as postulated by Hawley et al. (1936) that a highly alkaline urine would have lower amounts of vitamin C than a highly acid urine; the alkaline ash from the organic acids serving to retain the vitamin C in the blood and tissues where Nature had assigned it to guard against the many enemies of the body—the toxins and ferments of bacteria. As a result of avitaminosis C, liver glycogen is mobilized—glycogenolysis; and further storing of sugar in the liver is prevented—glycogenesis (Mackenzie, 1917). To further enhance the hyperglycemia this vasoconstriction brings about a decrease in the pancreatic secretions by lessening the amount of blood passing through the gland (Mann and McLachlan, 1917).

That the adrenal glands and vitamin C are closely allied in the defense of the body has been proven by experimentation and by autopsy. In normal persons any excess of vitamin C is excreted in the urine. In persons suffering with an acute infection, particularly a virus infection, vitamin C is not only absent from the urine but is also missing from the blood serum. This is true even when moderate amounts are given intravenously. These observations on serum were made with a Klett-Summerson photoelectric colorimeter using the method described by Mindlin and Butler. The observations on the urine were conducted according to the instructions of Goldsmith and Ellenger. Harde and Benjamin (1934-35) found the vitamin C fraction of the adrenal glands greatly reduced in monkeys killed or paralyzed by the virus of poliomyelitis. Yavorsky, Almoden and King (1934) reported identical findings in humans having died of various infectious agents.

This gives us an important concept of the value of vitamin C in virus diseases. The explanation for the absence of vitamin C in the infectious states is that this agent joins with the toxin and/or virus to form a new compound which is then destroyed by oxidation. Since the body is dependent on food for vitamin C to meet its daily needs, it is obvious that the body tissues would soon be depleted, and we would expect to find evidence of a prescor-

butic state in patients who had hypovitaminosis C. In patients seriously ill with a virus invader, the added strain on the capillaries by the application of a tourniquet, even for a few seconds, produced petechial hemorrhages at the site of constriction. Since not all patients thus demonstrated this capillary weakness, all patients ill with a virus infection were investigated by the aid of a petechiometer. Increased capillary fragility was found to exist in all cases, and the number of petechiae as expressed in centimeters of mercury followed the urine sugar findings. This deficiency syndrome was reversed as the glycosuria cleared, indicating that both were responsive to a proper plasma level for vitamin C.

At this same time the anaerobic conditions in the tissues will be relieved by the catalytic action of vitamin C acting as a gas transport to aid this cellular respiration. The abnormal acidity of the blood and tissues will be removed and abnormal amounts of free adrenalin will disappear from the blood stream. Following this the constriction of the blood vessels will cease, allowing the liver and pancreatic tissue to return to normal function. Continuance of frequent injections of properly calculated doses of vitamin C will restore the normal physiology of the body. This is not all of the story.

Lojkin (1937), studying the various phases of the inactivation of crystalline tobacco mosaic virus by 1-ascorbic acid, suggested that the action was not due to reduced vitamin C nor to the irreversibly oxidized dehydroascorbic acid. Lojkin felt that it was due to a specific intermediate product which is formed in the course of the catalytic auto-oxidation of vitamin C, an action stimulated by the presence of copper ions. This intermediate product must be a peroxide because a peroxide is formed during copper-catalyzed oxidation of vitamin C. This peroxide is decomposed as rapidly as it is formed (Barrow, De Meio, Klemperer, 1935-36). Lyman and associates (1937) confirmed the peroxide theory by observing that the oxygen uptake, beyond that calculated for the reaction ascorbic acid to dehydroascorbic acid, was not due to further oxidation of dehydroascorbic acid to an irreversible oxidation product, because treatment of the oxidized solution with hydrogen sulfide gave complete recovery of the ascorbic acid. These men also found that copper catalysis accelerates not only the reversible oxidation of vitamin C, but also further oxidation of dehydroascorbic acid. This action of the copper ion elucidates the findings that vitamin C in massive, frequent doses works better in the body than in a laboratory test tube.

Hippocrates declared the highest duty of medicine to be to get the patient well. He further declared that, of several remedies physicians should choose the least sensational. Vitamin C would seem to meet both these requirements.

THE JOURNAL OF SOUTHERN MEDICINE AND SURGERY

306 NORTH TRYON STREET, CHARLOTTE, N. C.

The Journal assumes no responsibility for the authenticity of opinion or statement made by authors, or in communications submitted to this Journal for publication.



JAMES M. NORTINGTON, M.D., Editor

VOL.CIII

APRIL, 1951

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F. R. KLENNER, M.D., Reidsville, North Carolina

IT has been reported that one of the mold-derived drugs, in addition to being a good antibiotic, is a super-vitamin. Conversely, we argue that vitamin C, besides being an essential vitamin, is a super-antibiotic. Vitamin C in vitro, if maintained at body temperature, inactivates certain toxins at an unbelievable rate. Five parts per thousand of vitamin C with toxins and appropriate controls, incubated at 37° C. for 48 hours showed when tested on mice the minimal lethal dose for the control tubes to be 1/16,000 c.c., while that from the mixture of vitamin C and toxin was only 1/1,000 of a c.c. (Klegler, Guggenheim, Warburg, 1938). In this study the loss of vitamin C in toxin broth and ordinary broth controls followed a constant pattern: the loss, however, was always greater in the toxin broth tube. The difference between the rate of disappearance of vitamin C in toxin and ordinary broth was more striking the greater the concentration of vitamin C. It is, therefore, reasonable to conclude that the degree of neutralization in a virus infection will be in proportion to the concentration of the vitamin and the length of time in which it is employed.

Since it has long been known that the virus organism resembles more the toxins and ferments than the common animate causes of disease, it would seem plausible that the detoxication effected

by vitamin C is produced by a direct combination of the vitamin with the toxin and/or virus, this followed by the oxidation of the new compound which destroys both the virus and/or toxin and the vitamin. This destruction of the virus by oxidation has been concurred in by many investigators. Since vitamin C is an integral part of the oxidation-reduction system of the body, its function in the role of an antibiotic becomes intelligible. To appreciate the antagonistic properties of vitamin C against the virus organism and the chemical ferments of exotoxin-producing microorganisms, one must forget its present academic status as a factor essential for life. A cow is valuable to the farmer not only for her ability to produce milk, but also as a source of organic fertilizer. Vitamin C, likewise, is important, not only as a detoxifying agent, as a catalyst aiding cellular respiration by acting as a hydrogen transport, as a catalyst in the assimilation of iron, and as a conservator of collagen fibers and bundles in tissues of mesenchymal origin; but, also, because of its function as a reducing agent or the precursor of such a substance. In this latter capacity it fulfills the requirements of an antibiotic. A striking phenomenon of vitamin C is the similarity of response, whether to correct pathologic processes due to a deficiency of this compound, acting as a vitamin; or to destroy the ferments of microorganisms, acting as an antibiotic. Within a few hours after institution of adequate vitamin C therapy to correct an avitaminosis, his-

Presented in the Fifty-second Annual Meeting of the Tri-State Medical Association of the Carolinas and Virginia, held at Columbia, February 19th and 20th, 1951.

tological evidence of bone improvement is obtainable. Fibroblasts begin to form normal connective tissue and capillary buds are invading hemorrhagic areas (Youmans, 1941). Similar is its dramatic antibiotic action, the rule being clear evidence of clinical response within a few hours.

The purpose of this paper is to present clinical proof of such action for this vitamin.

Case I is one of premeasles in a ten-months-old baby. The term "premeasles" is adopted to express the syndrome of fever, redness of eyes and throat, catarrh, spasmodic bronchial cough and Koplik spots. Vitamin C, 65 mgm. per Kg. of body weight, was injected intramuscularly every four hours. The fever dropped from 105 to 97.6° F. within 12 hours. All symptoms showed marked clearing. This sudden drop in the fever was thought to be explainable on one of three grounds: 1) Common right drop. 2) Due to the antibiotic action of vitamin C. 3) Even if the vitamin C administration had been continued, possibly a moderate rise would have occurred in the late afternoon of the second day, granting a highly virulent organism and a poorly resisting host. To determine which of these deductions was valid, vitamin C was discontinued for a period of eight hours. At this point the rectal temperature was back up to 103.4. Vitamin C therapy was resumed and instead of the expected 8 P.M. climb, the temperature was down to 99.2 (R) eight hours later. The vitamin C injections were continued, the baby made an uneventful recovery and was discharged 60 hours following admission. No measles rash developed. Eighteen months have elapsed since this illness and the child has not had clinical measles. This is not due to the establishment of active immunity but to the lack of a second exposure.

Case 2 confirms the previous case. This case is that of a 22-months-old infant with symptoms identical with that just described. The same medication was followed; the same clinical course followed. Under parental pressure the child was discharged from the hospital within 36 hours, apparently well. Four days later the child's brother and sister broke out with measles, which ran the usual course, having received no specific therapy. Seven days later the 22-months child broke out with measles. This time vitamin C was not given. The case was judged as modified.

The response as observed in measles was characteristic for vitamin C *versus* virus infections. Two cases of virus pneumonia complicated by encephalitis were so unusual that case histories are given.

Case 3 is that of a colored woman, aged 28, with history (given by a relative) of chills and fever and chest and head cold for 14 days, severe headache for three days. In stupor when first seen, eye lids closed, a white foam at the mouth which

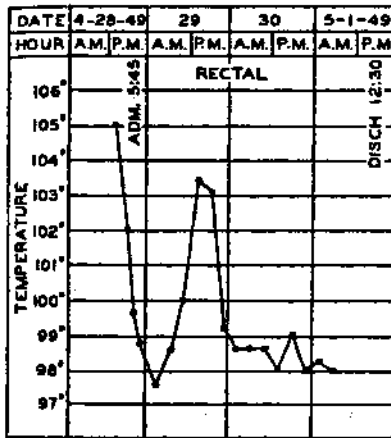
she periodically tried to spit out. Temperature by axilla 106.8. Dehydration was much in evidence, breath sounds diminished to absent, tactile fremitus increased over the entire right lung. The sulfa drugs, penicillin and streptomycin with supportive treatment had been exhausted. Four grams of vitamin C was given intravenously along with 1000 c.c. of 5 per cent dextrose in saline solution. Temperature dropped to 100 (Ax.) within 11 hours. Four hours later, vitamin C was resumed—every two to three hours, in dosage of 2 to 4 grams depending upon the response. After 72 hours the patient was awake, sitting up in bed and taking fluids freely by mouth. There was no fever at this time, nor for the remainder of the time in hospital. Vitamin C was continued for a period of two weeks; the frequency was cut to every 12 hours, two grams at a dose. An interesting complication was deafness; her speech gave a loud, monotonous, bell-sound effect. It was debated whether this was the result of the streptomycin or to the encephalitis. Prostigmin 1:2000, 1 c.c., and vitamin B₁, 200 mgm., were given IM twice daily. On the tenth day of treatment the hearing suddenly returned to normal. The x-ray picture of the right lung was one of almost complete consolidation. Although the patient was clinically well of her pneumonia after 72 hours, the x-ray picture was not completely clear until 90 days later.

This phenomenon of Nature clearing the debris after killing out the virus organism was observed in five other cases. The time required was in direct proportion to the degree of pulmonary involvement. There is nothing new about this procedure; Nature merely duplicating a stage in the metamorphosis of the frog in getting rid of its tadpole tail.

Case 4. that of a white baby 19 months old, bothered with a little cold for two weeks, not very sick until the last 24 hours, in which the baby had been "runnings high fever that could not be broken with aspirin." Clonic convulsive seizures of the right arm and leg began 12 hours before admission. An undernourished infant, lying rigid in its mother's arms, skin cold to touch, color cadaver-like, eyes closed, grade -2 mucopurulent nasal discharge, throat red. The temperature was 103.8 (R). Breath and heart sounds practically inaudible. Areas of skin over the back presented an appearance similar to that seen in rigor mortis.

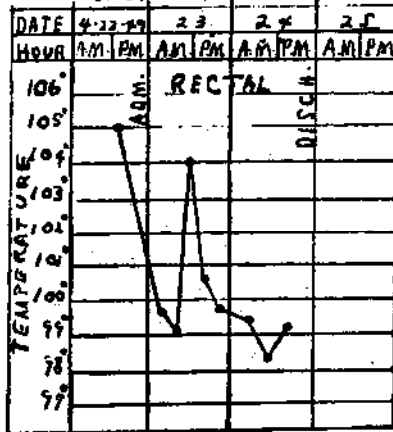
Vitamin C, 1000 mg., was given IM. repeated every four to six hours. At the first injection the baby did not move and the sensation was like that of sticking an orange. To give rapid external heat, mustard plasters were applied to the anterior and posterior chest in a mixture of one part mustard to three parts flour. A croup tent was set up. The vapor carrying compound tincture benzoin; 50

BABY D. S. (29753)



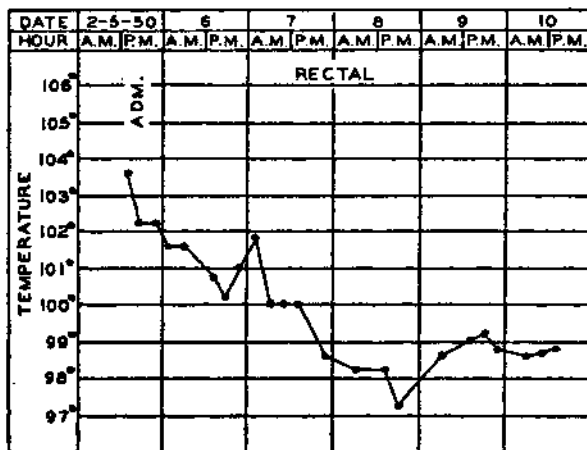
MEASLES

BABY J. S. D.



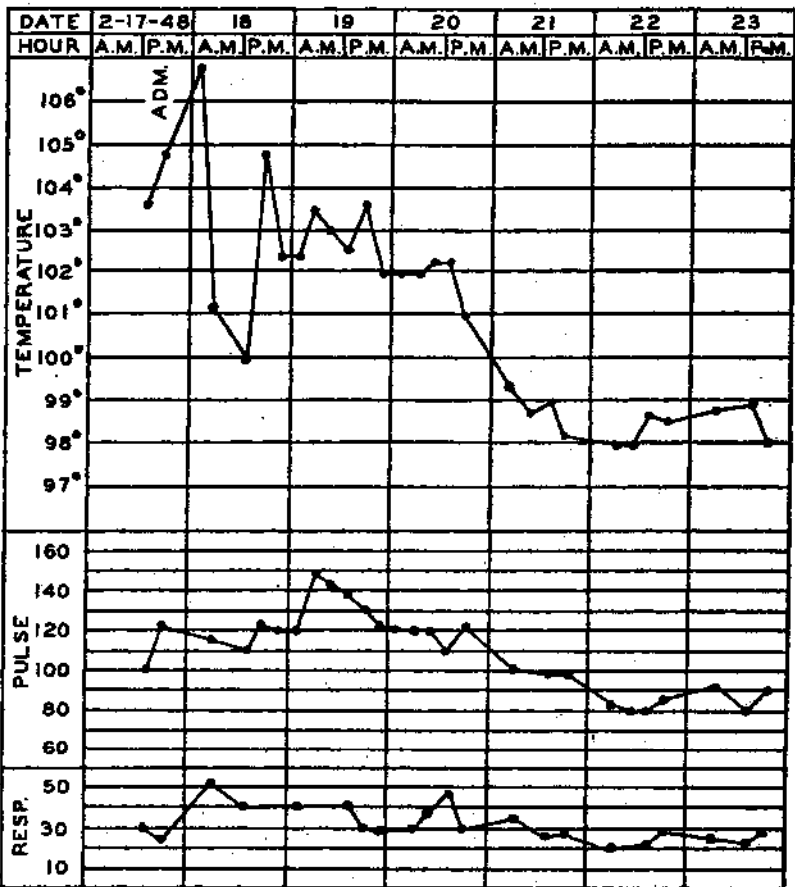
MEASLES

BABY W. M. (32219)



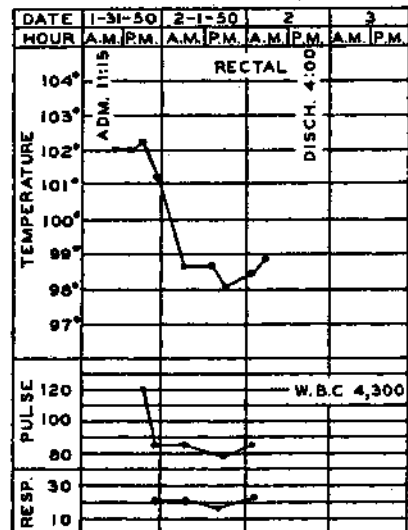
VIRUS ENCEPHALITIS-MENINGITIS

M. H. (26047)



VIRUS PNEUMONIA

L. R. (31880)



VIRUS INFECTION (PULMONARY)

c.c. of 5 per cent dextrose in saline was given under the skin in the scapular areas. Two hours after the first injection of vitamin C the baby drank 240 c.c. of orange juice, the first food of any type taken by the baby in 24 hours. This was repeated 1½ hours later. At this time there was total paralysis of the right arm and leg. Twelve hours after admission the baby moved his right leg and one hour later grasped a bottle of orange juice with both hands. From this point on the recovery was uneventful. Of secondary importance is the laboratory report of *Ascaris lumbricoides* ova and hemoglobin 55 per cent.

Cases 5 and 6 are of pulmonary virus infection, (a) in a boy of 14 years, and (b) in a man of 58 years. In the case of the boy the fever curve was of the type showing a fast response to heavy vitamin C injections. The WBC was 4,300, urine sugar ++. Twenty-six grams of vitamin C was given IV to this patient in a 44-hour period.

In the case of the man, Case 6, the fever decline was after a modified step-ladder fashion. In this instance the amount of vitamin C injected was less than half of the recommended dose. The WBC was 5,850, admission urine sugar +++. Thirty-one grams of vitamin C was injected intravenously over a period of 60 hours. It is to be noted that the same amount of vitamin C (2 grams every four hours) was given to the boy and to the man, disregarding the factor of body weight. Had the man received four or five grams every four hours, or two grams every two hours, his hospital course would probably have followed the same pattern as that of the boy. A point of great interest was that at subsequent examinations the urine was consistently negative for sugar. The course in these cases emphasizes the necessity of administering massive doses of vitamin C at frequent, regular intervals so as to maintain the proper level of this antibiotic in the tissues.

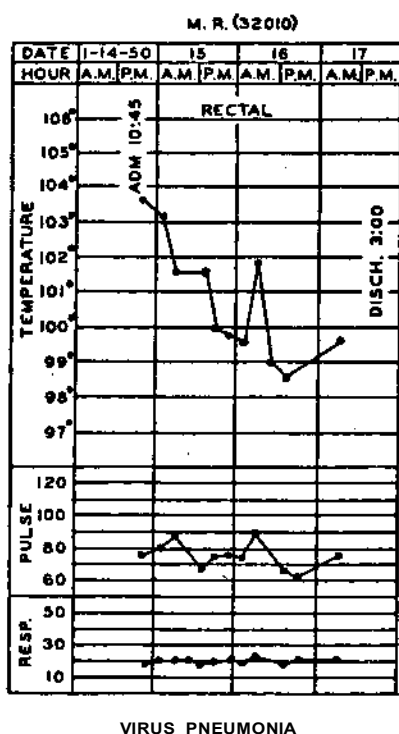
The amount of vitamin C for optimal effect will vary greatly with the individual. The type of the disease and the degree of toxemia are important guides in determining the dosage. Although the usual dose of vitamin C is calculated on the basis of 65 mgm. per Kg. of body weight, and given every two to four hours by needle, under certain conditions larger single injections can be used to good advantage. Vitamin C given to a child with measles, mumps or chickenpox will abort or modify the attack, depending upon the intensity of the treatment. If the activity of the pathogen is stopped, the development of active immunity will be interrupted. In handling these particular childhood diseases, when uncomplicated, the treatment should be aimed at modification of the infection as the plan of choice. To accomplish this end vitamin C should be increased to 250 mgm. per Kg. of

body weight, and the injection given intramuscularly. It will be necessary, at times, to repeat with half of this amount eight hours later. The vitamin was given in a concentration of 500 mg. per c.c. of solution. Pain was slight and lasted only a few minutes. Procaine, 0.5 to 2 per cent, instilled from a second syringe into the gluteal muscle through a placed needle just before giving the vitamin might solve this problem. The itch of measles and of chickenpox, the occasional vomiting of these illnesses, and the pain of mumps were fully controlled within one hour, when 250 mg./Kg. body weight was used. Instead of repeating waves of macules in chickenpox, and the usual seven to nine days required for crusting, following the heavy modifying injection no new eruptions appeared and crusting was present within six hours. Further clinical studies may prove that the routine use of the higher dose (250 mg./Kg. body wt.) replacing the usual (65 mg./Kg. body wt.) is indicated in all virus infections and the results produced may be even more dramatic.

The greatest value of vitamin C in virus infections does not rest with these lesser kinds of diseases, some of which, e.g. measles, can be modified or prevented by the proper use of immune globulin. The value above all others is its positive action against the virus causing poliomyelitis. A report of this usage was published in the official journal of this association in 1949. Many physicians refuse to employ vitamin C in the amounts suggested, simply because it is counter to their fixed ideas of what is reasonable; but it is not against their reason to try some new product being advertised by an alert drug firm. It is difficult for me to reconcile these two attitudes. On the other hand, many physicians who have been willing to try vitamin C against the virus of poliomyelitis have obtained the same striking results as we reported. Scores of letters from practitioners here in the United States and in Canada could be presented in evidence. In some instances doctors have cured their own children of poliomyelitis by giving vitamin C and in other cases doctors themselves have been cured.

In poliomyelitis vitamin C performs three important functions: 1) It destroys the virus; 2) acting as the dehydrator and diuretic of first choice, it removes the edema fluid from the brain and the cord; 3) it preserves the lining of the central canal and maintains more regular spacing and less crowding of the ependymal cells (Altman). The pressure within the bony vault of the central nervous system resulting from the inflammatory process excited by the virus, acts as a haemostat to cut off the blood supply to the anterior horn cells. This compression of their vessels denies to the horn cells the essentials for function, for life even.

It is of more than academic interest to review



the findings of McCormick in 50 confirmed cases of poliomyelitis in and around Toronto, Canada, during the epidemic of 1949. This report is that children of families eating brown bread who came down with poliomyelitis did not develop paralysis; whereas in those families eating white bread many of the children having poliomyelitis did develop paralysis. The point here is that brown bread has 28 times more vitamin B₁ than does white bread. Obviously, then, the paralysis which complicates acute poliomyelitis appears to be due to a B₁ avitaminosis. Vitamin C by removing edema fluid relieves from pressure these vessels that supply nutriment to the horn cells, thus allowing the normal complement of vitamin B₁ to reach these cells. In December, 1949, a 5-year-old white girl was brought to my office with paralysis of both lower extremities of 4½ days' duration. The child had been ill for 12 days. There was complete flaccid paralysis of the right leg, 85 per cent paralysis of the left leg. Pain was directed to the knee and to the lumbar back. In hospital the diagnosis of poliomyelitis was confirmed by four consulting physicians. Spinal fluid cells were 82. No medication of any type was given exclusive of vitamin C. Massage was started immediately. The rationale of using early massage had two bases: 1) In the course of general practice patients would give a history of having had poliomyelitis when a child and that their mother rubbed the paralyzed member day and night until function returned. 2) That paralyzed muscle was in profound shock and "artificial respiration" would maintain proper metabolism

during the emergency phase. To the first injection of vitamin C there was definite response. After 96 hours the child was moving both legs. The flexion was slow and deliberate. She was discharged from the hospital at this time, vitamin C being continued by mouth—1000 mg. every two hours with fruit juice for seven days. On the 11th day of treatment the child was walking about the house, but her gait was slow and her posture was poor, being bent forward. Vitamin C was discontinued and vitamin B₁ started—10 mg. before meals and bed hour. Carbonated drinks were encouraged for their sugar content and mild stimulating action. Nineteen days after starting treatment there was complete return of sensory and motor function which has persisted to this date.

A boy of eight years was brought to my office with a history of having had "flu" for a week, and four days previously having developed photophobia, conjunctivitis, sore throat, nausea, vomiting and a back-of-the-eyes type headache of such intensity that adult doses of aspirin had no effect. The boy was either rubbing his neck on the left side or holding his head between his hands, begging for something to relieve his pain. The fever was 104.4 (Ax.) He was tender in the lumbar region and he had a drawing sensation referred to the hamstring attachments at the knee. Two grams of vitamin C was given IV while in the office. He was then sent to the local hospital where he received promptly a second injection of 2 grams of the vitamin, after which it was given every four hours. Six hours after commencing therapy the neck pain was gone, the headache completely relieved, he could tolerate the ceiling light, his eyes were dry and the redness clearing. Nausea and vomiting had disappeared, the fever was down to 100.6 (Ax.), and he was sitting up in bed in a jovial mood while he drank a carbonated beverage. He was discharged from the hospital after receiving 26 grams of the vitamin in a 48-hour period, clinically well. Vitamin C was continued by mouth, 1500 mg. every two hours with fruit juice for one week, then change was made to vitamin B₁, 25 mg. before meals and bed hour. Vitamin B₁ in these cases should be continued for a period of no less than three months as nerve tissue is slow in recovering from damage.

In using vitamin C as an antibiotic minor complications were occasionally seen. These fall into six groups: 1) Diarrhea in two cases. In each instance the preparation contained sodium bisulfate. The enteritis cleared on giving a preparation of vitamin C not containing this salt. 2) Induration in 42 cases—seen either immediately following the injection (allergy), or delayed. In the latter it was found that the injections were being given too close to the surface. Applications of warm magnesium

sulfate as a compress gave prompt relief of the pain and swelling. In two of these cases fluctuation ensued and healing was effected by surgical drainage and the application of compresses. The impression in these two cases was that a vein had been opened by the needle. The exudate was dark and both the slide and culture studies were negative for bacteria. 3) Endothelial irritation in three cases. Acute pain radiated from the site of the injection to the shoulder. In each instance the concentration of the vitamin was one gram to each 5 c.c. solution and the amount given exceeded two grams. After slowing the rate of injection this reaction did not occur. 4) Venous thrombosis in one case. The concentration was 500 mg. per c.c. solution; the total dose 5 c.c. Compressing relieved the pain. The pathology was very similar to that following the use of 50 per cent dextrose solution. 5) Syncope—In maximum doses given IV a sensation of fainting and dyspnea occurred seven times. Five of these patients were over 55 years of age. The disagreeable symptoms were relieved by slowing the speed of the injections. 6) Rash—In three cases a pin-point dermatitis occurred, limited to the face and upper third of the torso, identical to that seen in infants taking orange juice. This did not necessitate discontinuance of therapy and cleared spontaneously several days after vitamin C was stopped.

Calcium, *in vivo*, duplicates the chemical behavior of vitamin C in many respects. Calcium gluconate and calcium lexulinate were used in conjunction with vitamin C therapy in a small series of pulmonary virus infections and in mild cases of influenza. There was a definite synergistic response. Patients with colds derived most benefit from this combined treatment. Because of its action on cardiac muscle, the use of calcium was limited to adults and the amount injected to two grams per day. One gram administered IV at moderate speed will so slow the heart as in many cases to produce syncope. If the concentration becomes great enough cardiac arrest in a tonically contracted state might result. It is, however, quite possible that, with the proper ionic balance of calcium and vitamin C in the same solution, larger amounts could be given without side effects. The massive dose schedule limits the usefulness of the calcium ion in virus diseases to that of an adjuvant only.

In all of the cases of virus infection reviewed in this study one laboratory finding stood out as of great significance. On admission to the hospital the first routine urine examination showed some degree of glycosuria. The pattern of the qualitative Benedict's reaction was constant enough to postulate that the higher the reading the more severe was the pathology. Repeat urine sugar studies following vitamin C therapy revealed complete clearing. This was true even though fruit juices were forced to tolerance. This finding confirmed the

knowledge that interference with the normal physiology of the adrenal glands, either by the toxins produced by microorganisms or by surgery, has a profound influence on metabolism, especially of the carbohydrates. Adrenalin in the blood stream causes hyperglycemia with resulting glycosuria. Adrenalin acts either by stimulation of the sympathetic nervous system or directly via the blood. This action of adrenalin is via the blood only, because the effect, as demonstrated in experimental animals, is still realized after destruction of the cord and sympathetic plexuses and degeneration of the peripheral post-ganglionic fibers (Evans, 1930). The glycosuria found in these cases was not due to a lowering of the threshold for sugar excretion by the kidney, paralleling a phloridzin diabetes, since the carbohydrate mechanism was associated with a hyperglycemia (Zuelzer, 1901, Metzger, 1902, Paton, 1903). Likewise there was no evidence of kidney damage. Albumin was reported negative and the microscopic examination showed no cells or casts. Apparently this is a condition of artificial diabetes mellitus, which would suggest the answer for the diabetic who loses ability to maintain sugar-insulin balance when embarrassed with an acute infection.

The story of a 7-year-old boy may have a lesson. He has been known to be diabetic since the age of four years. Any incident of infection in this lad produced an alarming interference of his sugar-insulin-diet equilibrium. Recently he contracted measles, and as the disease process developed toward its height the urine sugar curve swung sharply upward. From an occasional dose of 5 units regular insulin his requirement rose to 30 units regular insulin, three times each day, while still running a 3- or 4-plus Benedict's test. (Other forms of insulin proved by trial to be too dangerous.) At the peak of his infection vitamin C was started in a modifying dose of one gram every four hours. His general condition soon improved and in the course of several days he returned to his usual diet-insulin schedule and his usual urine sugar. In patients with diabetes, vitamin C should be discontinued just as soon as the temperature returns to normal. Prolonged use of vitamin C might prove undesirable due to its dehydrating and diuretic powers.

The pathologic process at work here is only compatible with abnormal amounts of adrenalin in the blood stream. It is not a response to an emotional stimulus to the adrenal medulla, since free adrenalin in the circulating blood has a transitory action, being so rapidly oxidized that none gets into the urine. This suggested that the regulator of the adrenalin mechanism had been removed, so that a constant supply of adrenalin would be present in the blood, making possible a concentration sufficiently high to cause constant vasoconstriction.

Ritzmann (1909) found that adrenalin affected carbohydrate metabolism only when this vasoconstriction phase existed. This finding was concurred in by Lusk (1914), who further concluded that this action on blood vessels caused asphyxia of the tissues which tended to increase the acidity of the blood and the tissues. This superimposed acidity further promotes the production of adrenalin hyperglycemia (Peters and Geyelin, 1917). McDannell and Underbill (1919), studying these phenomena in rabbits, found that slight hyperglycemia could be controlled by the administration of sodium carbonate.

The rationale of forcing fruit juices in the old treatment of colds was based on this theory as postulated by Hawley et al. (1936) that a highly alkaline urine would have lower amounts of vitamin C than a highly acid urine; the alkaline ash from the organic acids serving to retain the vitamin C in the blood and tissues where Nature had assigned it to guard against the many enemies of the body—the toxins and ferments of bacteria. As a result of avitaminosis C, liver glycogen is mobilized—glycogenolysis; and further storing of sugar in the liver is prevented—glycogenesis (Mackenzie, 1917). To further enhance the hyperglycemia this vasoconstriction brings about a decrease in the pancreatic secretions by lessening the amount of blood passing through the gland (Mann and McLachlan, 1917).

That the adrenal glands and vitamin C are closely allied in the defense of the body has been proven by experimentation and by autopsy. In normal persons any excess of vitamin C is excreted in the urine. In persons suffering with an acute infection, particularly a virus infection, vitamin C is not only absent from the urine but is also missing from the blood serum. This is true even when moderate amounts are given intravenously. These observations on serum were made with a Klett-Summerson photoelectric colorimeter using the method described by Mindlin and Butler. The observations on the urine were conducted according to the instructions of Goldsmith and Ellenger. Harde and Benjamin (1934-35) found the vitamin C fraction of the adrenal glands greatly reduced in monkeys killed or paralyzed by the virus of poliomyelitis. Yavorsky, Almoden and King (1934) reported identical findings in humans having died of various infectious agents.

This gives us an important concept of the value of vitamin C in virus diseases. The explanation for the absence of vitamin C in the infectious states is that this agent joins with the toxin and/or virus to form a new compound which is then destroyed by oxidation. Since the body is dependent on food for vitamin C to meet its daily needs, it is obvious that the body tissues would soon be depleted, and we would expect to find evidence of a prescor-

butic state in patients who had hypovitaminosis C. In patients seriously ill with a virus invader, the added strain on the capillaries by the application of a tourniquet, even for a few seconds, produced petechial hemorrhages at the site of constriction, since not all patients thus demonstrated this capillary weakness, all patients ill with a virus infection were investigated by the aid of a petechiometer. Increased capillary fragility was found to exist in all cases, and the number of petechiae as expressed in centimeters of mercury followed the urine sugar findings. This deficiency syndrome was reversed as the glycosuria cleared, indicating that both were responsive to a proper plasma level for vitamin C.

At this same time the anaerobic conditions in the tissues will be relieved by the catalytic action of vitamin C acting as a gas transport to aid this cellular respiration. The abnormal acidity of the blood and tissues will be removed and abnormal amounts of free adrenalin will disappear from the blood stream. Following this the constriction of the blood vessels will cease, allowing the liver and pancreatic tissue to return to normal function. Continuance of frequent injections of properly calculated doses of vitamin C will restore the normal physiology of the body. This is not all of the story.

Lojkin (1937), studying the various phases of the inactivation of crystalline tobacco mosaic virus by l-ascorbic acid, suggested that the action was not due to reduced vitamin C nor to the irreversibly oxidized dehydroascorbic acid. Lojkin felt that it was due to a specific intermediate product which is formed in the course of the catalytic auto-oxidation of vitamin C, an action stimulated by the presence of copper ions. This intermediate product must be a peroxide because a peroxide is formed during copper-catalyzed oxidation of vitamin C. This peroxide is decomposed as rapidly as it is formed (Barrow, De Meio, Klemperer, 1935-36). Lyman and associates (1937) confirmed the peroxide theory by observing that the oxygen uptake, beyond that calculated for the reaction ascorbic acid to dehydroascorbic acid, was not due to further oxidation of dehydroascorbic acid to an irreversible oxidation product, because treatment of the oxidized solution with hydrogen sulfide gave complete recovery of the ascorbic acid. These men also found that copper catalysis accelerates not only the reversible oxidation of vitamin C, but also further oxidation of dehydroascorbic acid. This action of the copper ion elucidates the findings that vitamin C in massive, frequent doses works better in the body than in a laboratory test tube.

Hippocrates declared the highest duty of medicine to be to get the patient well. He further declared that, of several remedies physicians should choose the least sensational. Vitamin C would seem to meet both these requirements.

NOTE:

**PubMed gives a different
Volume -number
compared with the one printed:**

Massive doses of vitamin C and the virus diseases.
South Med Surg. 1951 Apr;**113**(4):101-7. No abstract
available.
PMID: 14855098 [PubMed - indexed for MEDLINE]

Dr. Fred Klenner describes the use of injectable vitamin C as part of the treatment for lockjaw (tetanus) in a six-year-old boy. He also describes using injectable vitamin C to successfully treat a four-year-old child bitten by a mature highland moccasin. (Note also, he instructed the father of the snake-bitten child to call him every hour throughout the night to report on the child's condition following his first use of this treatment.)—*R.D.M.*

Recent Discoveries in the Treatment of Lockjaw with Vitamin C and Tolserol

Dr. Fred R. Klenner, Reidsville, N.C.
Tri-State Medical Journal, July 1954, Vol. 2, No. 2, pp. 7-11
Second in a Series of Two

The purpose of this paper is to dispel the popular belief that tetanus is a difficult disease to cure. It is bold, but correct to say that the number of cases terminating fatally from the disease are equaled by those who die from the treatment. Evidence will be presented to show that the antitoxin has no curative value and at the best is harmful. Convulsive seizures must be controlled, but it is wrong to employ a drug for this purpose that tends to deprive the patient of his sensorium. Many patients have been lost, not only with tetanus but also from the many other disease conditions, simply because the treating physician blindly followed a recommendation set down by a colleague who by "Fate" was in a position of authority. Too few of those who write appreciate the responsibility of their words. Unfortunately, in medicine, the driver's seat is still at the back. It is rare, indeed, to find any two authorities offering the identical treatment for any given disease. Some much used volumes give five, ten, or even fifteen different remedies for a given disease; this can only lead to "coin tossing." Yet MAN in his search for health still comes to the doctor. This condition will prevail until we assume enough courage to have but ONE textbook for the practice of medicine; this should be loose-leaf.

Case History: White boy of 6 years. Did not receive the required pre-school injections. Severe asthmatic since infancy. Reported to have had diphtheria March 1951; no smears or culture made. Present illness thought to have started three weeks before admission with severe attack of asthma which lasted for two weeks. This episode was associated with abdominal cramps, unexplained at the time, and a generalized sensation of muscle tightness. Six days before admission he developed drooping of the eyelids. He also found it difficult to smile (perpetual with this boy under normal circumstances) and there was definite resistance whenever he attempted to fully open his mouth, like in a yawn. Abdominal cramps were now more pronounced and they were experienced more frequently. Two days prior to admission his abdominal muscles assumed boardlike

rigidity which was synchronized with the abdominal pain and these episodes were being experienced more often while increasing in duration. His diet was self limited to liquids due to the inability to open his mouth more than 30%; this created pain at the temporomaxillary joint and was always followed by the sudden "involuntary" clamping of his jaws. On the day of admission he had progressed to a stage when the slightest stimulation would contract his back muscles with such force that he would form an arch with his body resting on his feet and head. Sweating was profuse during this time; respirations were absent. When the clonic spasm was released he would lie limp and exhausted.

The physical examination added little to this picture. The temperature was 100.4° F., respirations shallow 20 to 25 per minute, the pulse was rapid but not thready, running between 120 and 130. He could "push" his tongue to the margin of his lips and a facial expression was impossible. A few "terminal rales" could be heard in both lung fields. The right patellar reflex was exaggerated and since this elicited a convulsive seizure the other reflexes were not attempted. His course in the hospital was interesting but not dramatic. The most trying period was spent in combating the pathology resulting from allergy. There was a history of a fall in the pony yard resulting in "brush burns" of his hands about one week before the onset of the "peculiar asthma attack." (It must be added that many a devout person offered sincere prayer for this lad's recovery. I humbly submit that Providence in hearing these supplications, did employ my intellect in carrying out His design.)

In the past it was thought that successful therapy depended upon four factors: (1) Early and adequate use of antitoxin; (2) Sedation to the point of narcosis; (3) Wound debridement; (4) Competent, intelligent, continuous nursing; (5) Five percent hydrogen peroxide to which Tr. of iodine has been added for cleansing the wound, magnesium sulfate given intravenously as a 20% solution in the amount of 50 cc, curare, frequent warm baths, spinal tap with replacement of fluid with anti-tetanus serum and a quiet, dark room.

Today the treatment of tetanus has resolved itself into a plan best suited to combat the convulsive seizures. Except for one single dose of antitoxin (75,000 units) given deep intramuscularly above the portal of entry if this is known or is possible, the use of this "agent" should be forgotten. Its employment, presently, is intended more for the legal protection of the attending physician rather than for the betterment of the patient. Our case will prove that it has no value and in all probability was harmful. Teale and Embleton reported that the toxin does not pass from the capillaries to the tissue of the central nervous system, nor from the choroid plexus to the cerebrospinal fluid, and that it is blocked from reaching the cord along the afferent nerves by the posterior root ganglia. By inference they concurred with Meyer and Ransom in believing that the path taken by the poison was the motor nerves. MacCallum pointed out that the antitoxin cannot travel from the circulation into the nervous system and that unless it be injected into the nervous tissue, it is relatively valueless. Meyer and Ransom showed that the injection of antitoxin into the nerve ABOVE the point of inoculation would BLOCK and neutralize the toxin. Davison advocates the use of tetanus toxoid 0.1 cc given intradermally for five consecutive days as a means of boosting the patient's antitoxin titer.

The most important therapeutic measures available are massive doses of vitamin C and Tolserol, both given intravenously. Jungeblut reported that vitamin C, when added to tetanus toxin "in vitro," brings about inactivation of the toxin. He felt, however, that the mechanism of the inactivation of tetanus toxin by vitamin C was fundamentally different from that of toxin-antitoxin reactions. In one experiment he observed that guinea pigs injected with a mixture containing critical amounts of toxin and vitamin C died with tetanus if the mixture was not incubated and LIVED if the mixture was previously incubated. (We believe the human body to be a first class incubator.) This work of Jungeblut followed, in a fashion, the findings of Imamura who, in 1929, reported inactivation of tetanus toxin by adding it to ovarian follicular fluid. Corpus luteum is now known to contain a high concentration of vitamin C. We have found massive doses of vitamin C to be dramatically effective in hundreds of cases in which the offending poison was an exotoxin or a virus. (Here I must inject the story of a four-year-old child bitten on the leg by a mature, highland mocassin. This case is related to tetanus in that both conditions offer the "exotoxin" as the killing agent. The child was bitten at 7 p.m. while playing in the yard. Seen in the emergency room of the local hospital at 7:30 p.m., she was vomiting, was crying because of severe pain in her leg which she held above the "fang marks" and had a 99.2° F. fever. Four grams of vitamin C was given intravenously at 7:35 p.m. The following 35 minutes was taken up preparing and skin testing anti-venom serum which was given at 8:00 p.m. At this time and before the anti-venom was administered she had stopped vomiting, had stopped crying and was sitting on the emergency room table laughing while she drank an orangeade. Her comment was: "Come on, daddy, I'm all right now." She was not admitted to the hospital but was allowed to return home with the understanding that the father would give me a report, by telephone, each hour throughout the night. This he did. His report each time was that she was sleeping as she usually did, and that other than a small amount of swelling up to the calf of her leg, appeared normal. She was seen in my office the following morning at 10 a.m. At this time she had ½ degree of fever and about the same amount of swelling described by her father during the night reports. She had had a "big" breakfast and wanted to know if she could play when she returned home. She was given 4 grams of vitamin C intravenously and sent home. Seen the same day at 5:00 p.m. she had no fever and about the same amount of swelling. She was given 4 grams of vitamin C intravenously. The following morning, 38 hours after being bitten, she was completely normal. As a precautionary measure 4 grams of vitamin C was given intravenously. This was the end of the snake bite, except that she carried the fang marks for a considerable time. No other antibiotic was given for secondary wound invaders as a result of the bite and none was required. This treatment was first worked out by me in dogs and published in hunting and fishing magazines. Several physicians have cured rattlesnake bites using this treatment schedule; their voluntary letters are in my files.) The vitamin must be given by needle in massive doses and around the clock to obtain these results.

Intravenous TOLSEROL, given in adequate amounts, has no equal in controlling the convulsive seizures found in tetanus. In our case of the six-year-old boy weighing 20 Kg. we gave as an initial dose 200 mg of Tolserol in 500 cc of D5 water at a rate of 35 drops

per minute. Since no dose schedule was available for children at that time (September 1951), we experimented with this amount since we did not desire too great a relaxation. Prostigmin was made available for this emergency. There was no response to this amount of Tolserol, so after six hours an additional 800 mgm was given, using the same type of diluent. The results obtained proved that this was the drug of choice in producing relaxation and preventing convulsive seizures in tetanus. This fact was apparent before the fluid run was completed. Subsequent doses of Tolserol were set at 1000 mgm. This amount gave complete control of all muscle spasm for a period of 60 hours. Under the influence of intravenous Tolserol the patient immediately began to take nourishment by mouth, was not disturbed by noises in excess of what should be expected in a hospital and did not require a darkened room. Nursing care was limited to that given by "floor nurses," although we did keep a companion in the room at all times as a psychological measure. The same day that intravenous Tolserol was given the patient played with toys in his bed and used crayons to color pictures in a color book. After about 60 hours this interest was suddenly lost and mild spasms returned. This pattern was just as suddenly reversed by giving another 1000 mgm of Tolserol intravenously. Other types of therapy were employed in this case. A review of his hospital course will argue the case for vitamin C and intravenous Tolserol. At only one period of his hospitalization was the outcome in doubt and this was due to a reaction to serum. Here again Tolserol and vitamin C saved the day.

He was admitted 9/1/51 at 30 minutes past noon. Two grams vitamin C were given intravenously at 1:00 p.m. Liquids taken freely throughout afternoon. 6:00 p.m. 2 grams of vitamin C. (All vitamin C and Tolserol given in this case was administered intravenously.) At 8:15 p.m. child reported crying loudly. A.S.A. grains V given by mouth with some difficulty. 9:00 p.m. 2 grams of vitamin C. At 10:40 p.m. an S.S. enema was given with good results. The procedure did not excite muscle spasm. 12:00 midnight 4 grams of vitamin C and one 10 cc ampule calcium gluconate. Child sleeping. At 3:00 a.m. 4 grams vitamin C. Patient having moderate abdominal cramps; no difficulty in swallowing. 6:00 a.m. condition same; given 4 grams vitamin C. 8:00 a.m. some difficulty in swallowing; 4 grams vitamin C given at 9:00 a.m. and by 10:00 a.m. was resting quietly. Sleeping at 11:00 a.m. and at 12:00 noon voided 100 cc urine. (From this point kidney output was normal.) Taking fluids freely by mouth. At 1:00 p.m. 4 grams vitamin C and 600,000 units procaine penicillin. The entire afternoon was spent "lying quietly" in bed. Fluids now protinal in milk and egg in milk; no difficulty in swallowing. At 6:00 p.m. and 9:00 p.m. 4 grams of vitamin C. Nembutal suppository grains 2 ordered by intern but there was no restlessness. The explanation for this order was "so the boy would get off early to sleep." At 12:00 midnight was given aspirin grains V, 4 grams of vitamin C and 600,000 units procaine penicillin. The rationale of the penicillin was to prevent secondary pulmonary pathology. The night of September 3rd was uneventful; he received 4 grams of vitamin C at 3:00 a.m. and at 6:00 a.m. Had mild abdominal cramps, off and on, through the morning. At 10:00 a.m. 4 grams of vitamin C; sleeping at intervals. Because of "outside pressure" 25,000 units TAT were given with saline intravenously, after skin testing for sensitivity. This was at 12 noon. By 1:00 p.m. his temperature was up to 101° F. rectally, the highest since admission; refused egg in milk. 2:00 p.m. voided 300 cc urine. At 3:00

p.m. he was crying because of severe pain in his abdomen. Floor nurse reported in her daily log—"an uncomfortable period since antitoxin." 4:00 p.m. 4 grams vitamin C, refused all liquids but by 5:00 p.m. was sleeping. Since antitoxin therapy was not our decision we elected to be heroic and give it a test to prove its lack of value.

(I will never forget a case of "lockjaw" in an adult white female that was my duty to treat as a house physician at Moore County General Hospital in 1937. Notes which I made at that time show that this patient died from asphyxia less than one hour after receiving 30,000 units of tetanus antitoxin intravenously. The serum was not diluted in saline as we employed in this case but it was given very slowly. Intravenous sodium amytal failed to release the convulsive seizure in this woman.)

At 8:00 p.m. 50,000 units T.A.T. in saline given intravenously; 4 grams of vitamin C given after completion of antitoxin. 9:00 p.m. he was, as before when T.A.T. was given, crying because of severe abdominal pain; his back was rigid and bowed. This picture continued fairly constant until 12:00 midnight; 4 grams vitamin C and 600,000 units penicillin given. By 1:00 a.m. he was resting comfortably and by 2:00 a.m. the nurse recorded—"abdomen more relaxed, still has slight attacks of pain but much further apart." 4:00 a.m. 4 grams vitamin C and he slept until bath at 7:00 a.m. At 8:00 a.m. 50,000 units T.A.T. intravenously in saline: aspirin grains V. 9:00 a.m. was having frequent sharp abdominal pain; nourishment by mouth was a bottle of carbonated drink and $\frac{1}{2}$ glass of milk. 12:00 noon 4 grams vitamin C and 4 grams again at 4:00 p.m. Comfortable throughout afternoon. At 7:30 p.m. 20,000 units tetanus antitoxin and crying out because of severe abdominal pain by 9:00 p.m.; refused all fluids by mouth. At 11:30 p.m. 500 cc 10% glucose in saline containing 4 grams vitamin C. September 5th. Attacks of muscle spasm more severe than at any other time. 12:00 midnight, 600,000 units procaine penicillin and 4 grams vitamin C; same amount of the vitamin at 4:00 a.m. and 8:00 a.m. Fairly normal sleep from 3:00 a.m. to 7:00 a.m. At 9:00 a.m. 300,000 units T.A.T. in saline intravenously; severe convulsive-like seizures of abdominal and back muscles reported at 11:00 a.m. 12:00 noon 4 grams vitamin C; sleeping quietly by 1:00 p.m. Oil retention enema given at 2:00 p.m. but unable to retain. Because of very severe seizures in which patient's body arched off the bed which was accompanied by profuse sweating we decided that if our little patient was to live some NEW type therapy must be adopted. Accordingly, 200 mgm of Tolserol in 500 cc D5 in water was started, the flow being 35 drops per minute. (This was an experimental dose since we could find no reports on the use of Tolserol intravenously in children.) 8:00 p.m. 4 grams vitamin C and 30,000 units tetanus antitoxin in saline at 9:00 p.m. Crying because of severe abdominal pain at 10:30 p.m.; also very restless and absolutely unable to swallow. September 6th. 12:00 midnight, 4 grams vitamin C and 600,000 units procaine penicillin. No response was observed after 6 hours with the 200 mgm. of Tolserol, so we elected to give 800 mgm. Tolserol in 500 cc D5 in water at this time, employing the 35 drops per minute schedule. 1:00 a.m. patient was resting quietly; asleep at 1:30 a.m. This continued until bath at 7:00 a.m. except for an occasional interruption caused by asking the patient how he felt. This was done to evaluate the degree of relaxation present; each time he responded gently that he was "feeling fine" and then returned to his slumbers. Vitamin C now given at 12-hour intervals maintaining the same dose

schedule. 12:45 p.m. 20,000 units T.A.T in 5% glucose in water and at 9:00 p.m. 28,000 units tetanus antitoxin in saline, both intravenously. It was of great significance to note that this time there were no exacerbations of muscle spasms—the Tolserol was doing a good job. September 7th was relatively uneventful. Three cc aqueous solution adrenal cortex was given every 8 hours for three times to relieve the strain on this gland. 5:00 p.m., we really began to hear from our tetanus antitoxin as the first urticarial wheel appeared on patient's right forearm. Benadryl 10 mg. and Kutapressin $\frac{1}{2}$ cc were given intramuscularly; one hour later 20 mgm benadryl and 3 mm adrenalin. Calamine lotion with phenol to whelps which by 9:00 p.m. had covered the entire body. Adrenalin 3 mm and benadryl 10 mg were given every 30 to 60 minutes, alternating, until 2:00 a.m. following day. Calcium gluconate 10 cc given intravenously. In spite of this therapy the stimulation from this serum reaction was enough to re-excite the muscles into painful spasms. At 11:30 p.m. 1000 mgm Tolserol in 500 cc 5% glucose in water was started. It was a rough night. By 3:00 a.m. the Tolserol was taking hold and "all was well" by 6:00 in the morning. Following this episode streptomycin was substituted for the penicillin in the light that it, too, might have played a part in the allergy. From this time until discharge Kutapressin, benadryl, and B-Complex were employed freely. Intradermal tetanus toxoid was given daily the last five days in the hospital. From this day on nourishment was taken freely when offered and muscle pain and spasm was absent. He was discharged on the 18th hospital day but could have safely returned home 10 days before. This we did not know at the time.

Vitamin C was employed for the following reasons: (1) Its antihistamine like action; (2) For its diuretic effect; (3) For its ability to neutralize exotoxins; (4) For its role in antibody formation. It is interesting to note that on September 8th, 10 days before discharge, the white blood count was 4,800 and the differential showed 45% lymphocytes and 55% polymorphs. Kracke states that one of the most notable instances of the increase of lymphocytes above normal is in recovery from acute infections. Kracke reports that Wintrobe gives as a fact: "That the lymphocytes are active in antibody formation."

In summary the following schedule will serve well in the treatment of TETANUS: (1) A debridement if a "ragged" wound is present; (2) Clean the field well. Any good antiseptic, applied thoroughly, will serve to sterilize the field. (Ether is too seldom used. It will destroy most bacteria, even colon bacillus, without injuring protoplasm.) Sterilizing of the wound when present, is done, not so much against the bacillus tetani which is highly resistant but for the destruction of other pathogenic or even non-pathogenic organisms: Park and Williams report that it has been found that pure cultures of tetanus, after the germs have sporulated and the toxins been destroyed by heat, can be injected into animals without producing tetanus. But if pathogenic strepto-cocci or staphylococci or even non-pathogenic organisms are injected simultaneously with the spores, or if there is an effusion of blood at the point of injection, or if there was a previous or later bruising of the tissues, the animals surely die of tetanus. The spores under such conditions can develop and produce the disease. For this reason one should give 75,000 units antitoxin deep intramuscularly above the wound when present and when possible. (3) Intravenous fluids; (4) intradermal tetanus toxoid 0.1 cc for five consecutive days; (5) massive doses of vitamin C around the clock and given by needle; (6) intravenous

Tolserol in adequate amounts. In our case 1000 mgm for a body weight of 20 Kg. was adequate. One can only hope that all the states will adopt legislation requiring annual booster injections of tetanus toxoid for all people regardless of age. This to be given at the expense of the states with the co-operation of its practicing physicians.

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Recent Discoveries in the Treatment of Lockjaw with Vitamin C and Tolserol

By DR. FRED R. KLENNER
Reidsville, N. C.

SECOND IN A SERIES OF TWO

The purpose of this paper is to dispel the popular belief that tetanus is a difficult disease to cure. It is bold, but correct to say that the number of cases terminating fatally from the disease are equaled by those who die from the treatment. Evidence will be presented to show that the antitoxin has no curative value and at the best is harmful. Convulsive seizures must be controlled, but it is wrong to employ a drug for this purpose that tends to deprive the patient of his sensorium. Many patients have been lost, not only with tetanus but also from the many other disease conditions, simply because the treating physician blindly followed a recommendation set down by a colleague who by "Fate" was in a position of authority. Too few of those who write appreciate the responsibility of their words. Unfortunately, in medicine, the driver's seat is still at the back. It is rare, indeed, to find any two authorities offering the identical treatment for any given disease. Some much used volumes give five, ten, or even fifteen different remedies for a given disease; this can only lead to "coin tossing." Yet MAN in his search for health still comes to the doctor. This condition will prevail until we assume enough courage to have but ONE textbook for the practice of medicine; this should be loose-leaf.

Case History: White boy of 6 years. Did not receive the required pre-school injections. Severe asthmatic since infancy. Reported to have had diphtheria March 1951; no smears or culture made. Present illness thought to have started three weeks before admission with severe attack of asthma which lasted for two weeks. This episode was associated with abdominal cramps, unexplained at the time, and a generalized sensation of muscle tightness. Six days before admission he developed drooping of the eyelids. He also found it difficult to smile (perpetual with this boy under normal circumstances) and there was definite resistance whenever he attempted to fully open his mouth, like in a yawn.

Abdominal cramps were now more pronounced and they were experienced more frequently. Two days prior to admission his abdominal muscles assumed boardlike rigidity which was synchronized with the abdominal pain and these episodes were being experienced more often while increasing in duration. His diet was self limited to liquids due to the inability to open his mouth more than 30%; this created pain at the temporomaxillary joint and was always followed by the sudden "involuntary" clamping of his jaws. On the day of admission he had progressed to a stage when the slightest stimulation would contract his back muscles with such force that he would form an arch with his body resting on his feet and head. Sweating was profuse during this time; respirations were absent. When the clonic spasm was released he would lie limp and exhausted.

The physical examination added little to this picture. The temperature was 100.4° F., respirations shallow 20 to 25 per minute, the pulse was rapid but not thready, running between 120 and 130. He could "push" his tongue to the margin of his lips and a facial expression was impossible. A few "terminal rales" could be heard in both lung fields. The right patellar reflex was exaggerated and since this elicited a convulsive seizure the other reflexes were not attempted. His course in the hospital was interesting but not dramatic. The most trying period was spent in combating the pathology resulting from allergy. There was a history of a fall in the pony yard resulting in "brush burns" of his hands about one week before the onset of the "peculiar asthma attack." (It must be added that many a devout person offered sincere prayer for this lad's recovery. I humbly submit that Providence in hearing these supplications, did employ my intellect in carrying out His design.)

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the point of narcosis; (3) Wound débridement; (4) Competent, intelligent, continuous nursing; (5) Five percent hydrogen peroxide to which Tr. of iodine has been added for cleansing the wound, magnesium sulfate given intravenously as a 20% solution in the amount of 50 cc, curare, frequent warm baths, spinal tap with replacement of fluid with anti-tetanus serum and a quiet, dark room.

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But if pathogenic streptococci or straphylococci or even non-pathogenic organisms are injected simultaneously with the spores, or if there is an effusion of blood at the point of injection, or if there was a previous or later bruising of the tissues, the animals surely die of tetanus. The spores under such conditions can develop and produce the disease. For this reason one should give 75,000 units antitoxin deep intramuscularly above the wound when present and when possible. (3) Intravenous fluids; (4) intradermal tetanus toxoid 0.1 cc for five consecutive days; (5) Massive doses of vitamin C around the clock and given by needle; (6) intravenous Tolserol in adequate amounts. In our case 1000 mgm for a body weight of 20 Kg. was adequate. One can only hope that all the states will adopt legislation requiring annual booster injections of tetanus toxoid for all people regardless of age. This to be given at the expense of the states with the co-operation of its practicing physicians.

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Tri-State Medical Journal

Published Monthly by the
TRI-STATE MEDICAL ASSOCIATION
with offices at
122 S. Greene St., Greensboro, N. C.
R. B. DAVIS, M.D., *Editor*

VOLUME II

JULY 1954

NUMBER 5

CONTENTS

President's Message	<i>Fred Kredel</i>	5
Editorial—Is It Becoming a Habit?	<i>R. B. Davis</i>	6
Recent Discoveries in the Treatment of Lockjaw with Vitamin C and Tolserol	<i>Fred C. Klenner</i>	7 — 11
Venom Poisoning	<i>Leon J. Taubenhau</i>	12

Recent Discoveries in the Treatment of Lockjaw with Vitamin C and Tolserol

By DB. FRED R. KLENNER
Reidsville, N. C.

SECOND IN A SERIES OF TWO

The purpose of this paper is to dispel the popular belief, that tetanus is a difficult disease to cure. It is bold, but correct to say that the number of cases terminating fatally from the disease are equaled by those who die from the treatment. Evidence will be presented to show that the antitoxin has no curative value and at the best is harmful. Convulsive seizures must be controlled, but it is wrong to employ a drug for this purpose that tends to deprive the patient of his sensorium. Many patients have been lost, not only with tetanus but also from the many other disease conditions, simply because the treating physician blindly followed a recommendation set down by a colleague who by "Tate" was in a position of authority. Too few of those who write appreciate the responsibility of their words. Unfortunately, in medicine, the driver's seat is still at the back. It is rare, indeed, to find any two authorities offering the identical treatment for any given disease. Some much used volumes give five, ten, or even fifteen different remedies for a given disease; this can only lead to "coin tossing." Yet MAN in his search for health still comes to the doctor. This condition will prevail until we assume enough courage to have but ONE textbook for the practice of medicine; this should be loose-leaf.

Case History: White boy of 6 years. Did not receive the required pre-school injections. Severe asthmatic since infancy. Reported to have had diphtheria March 1951; no smears or culture made. Present illness thought to have started three weeks before admission with severe attack of asthma which lasted for two weeks. This episode was associated with abdominal cramps, unexplained at the time, and a generalized sensation of muscle tightness. Six days before admission he developed drooping of the eyelids. He also found it difficult to smile (perpetual with this boy under normal circumstances) and there was definite resistance whenever he attempted to fully open his mouth, like in a yawn.

Abdominal cramps were now more pronounced and they were experienced more frequently. Two days prior to admission his abdominal muscles assumed boardlike rigidity which was synchronized with the abdominal pain and these episodes were being experienced more often while increasing in duration. His diet was self limited to liquids due to the inability to open his mouth more than 30%; this created pain at the temperomaxillary joint and was always followed by the sudden "involuntary" clamping of his jaws. On the day of admission he had progressed to a stage when the slightest stimulation would contract his back muscles with such force that he would form an arch with his body resting on his feet and head. Sweating was profuse during this time; respirations were absent. When the clonic spasm was released he would lie limp and exhausted.

The physical examination added little to this picture. The temperature was 100.4° F., respirations shallow 20 to 25 per minute, the pulse was rapid but not thready, running between 120 and 130. He could "push" his tongue to the margin of his lips and a facial expression was impossible. A few "terminal rales" could be heard in both lung fields. The right patellar reflex was exaggerated and since this elicited a convulsive seizure the other reflexes were not attempted. His course in the hospital was interesting but not dramatic. The most trying period was spent in combating the pathology resulting from allergy. There was a history of a fall in the pony yard resulting in "brush burns" of his hands about one week before the onset of the "peculiar asthma attack." (It must be added that many a devout person offered sincere prayer for this lad's recovery. I humbly submit that Providence in hearing these supplications, did employ my intellect in carrying out His design.)

In the past it was thought that successful therapy depended upon four factors: (1) Early and adequate use of antitoxin; (2) Sedation to

the point of narcosis; (3) Wound debridement; (4) Competent, intelligent, continuous nursing; (5) Five percent hydrogen peroxide to which Tr. of iodine has been added for cleansing the wound, magnesium sulfate given intravenously as a 20% solution in the amount of 50 cc, curare, frequent warm baths, spinal tap with replacement of fluid with anti-tetanus serum and a quiet, dark room.

Today the treatment of tetanus has resolved itself into a plan best suited to combat the convulsive seizures. Except for one single dose of antitoxin (75,000 units) given deep intramuscularly above the portal of entry if this is known or is possible, the use of this "agent" should be forgotten. Its employment, presently, is intended more for the legal protection of the attending physician rather than for the betterment of the patient. Our case will prove that it has no value and in all probability was harmful. Teale and Embleton reported that the toxin does not pass from the capillaries to the tissue of the central nervous system, nor from the choroid plexus to the cerebrospinal fluid, and that it is blocked from reaching the cord along the afferent nerves by the posterior root ganglia. By inference they concurred with Meyer and Ransom in believing that the path taken by the poison was the motor nerves. MacCallum pointed out that the antitoxin cannot travel from the circulation into the nervous system and that unless it be injected into the nervous tissue, it is relatively valueless. Meyer and Ransom showed that the injection of antitoxin into the nerve ABOVE the point of inoculation would BLOCK and neutralize the toxin. Davison advocates the use of tetanus toxoid 0.1 cc given intradermally for five consecutive days as a means of boosting the patient's antitoxin titer.

The most important therapeutic measures available are massive doses of vitamin C and Tolserol, both given intravenously. Jungeblut reported that vitamin C, when added to tetanus toxin "in vitro," brings about inactivation of the toxin. He felt, however, that the mechanism of the inactivation of tetanus toxin by vitamin C was fundamentally different from that of toxin-antitoxin reactions. In one experiment he observed that guinea pigs injected with a mixture containing critical amounts of toxin and vitamin C died with tetanus if the mixture was not in-

cubated and LIVED if the mixture was previously incubated. (We believe the human body to be a first class incubator.) This work of Jungeblut followed, in a fashion, the findings of Imamura who, in 1929, reported inactivation of tetanus toxin by adding it to ovarian follicular fluid. Corpus luteum is now known to contain a high concentration of vitamin C. We have found massive doses of vitamin C to be dramatically effective in hundreds of cases in which the offending poison was an exotoxin or a virus. (Here I must inject the story of a four-year-old child bitten on the leg by a mature, highland mocassin. This case is related to tetanus in that both conditions offer the "exotoxin" as the killing agent. The child was bitten at 7 p.m. while playing in the yard. Seen in the emergency room of the local hospital at 7:30 p.m., she was vomiting, was crying because of severe pain in her leg which she held above the "fang marks" and had a 99.2° F. fever. Four grams of vitamin C was given intravenously at 7:35 p.m. The following 35 minutes was taken up preparing and skin testing anti-venom serum which was given at 8:00 p.m. At this time and before the anti-venom was administered she had stopped vomiting, had stopped crying and was sitting on the emergency room table laughing while she drank an orangeade. Her comment was: "Come on, daddy, I'm all right now." She was not admitted to the hospital but was allowed to return home with the understanding that the father would give me a report, by telephone, each hour throughout the night. This he did. His report each time was that she was sleeping as she usually did, and that other than a small amount of swelling up to the calf of her leg, appeared normal. She was seen in my office the following morning at 10 a.m. At this time she had ½ degree of fever and about the same amount of swelling described by her father during the night reports. She had had a "big" breakfast and wanted to know if she could play when she returned home. She was given 4 grams of vitamin C intravenously and sent home. Seen the same day at 5:00 p.m. she had no fever and about the same amount of swelling. She was given 4 grams of vitamin C intravenously. The following morning, 38 hours after being bitten, she was completely normal. As a precautionary measure 4 grams of vitamin C was given intra-

venously. This was the end of the snake bite, except that she carried the fang marks for a considerable time. No other antibiotic was given for secondary wound invaders as a result of the bite and none was required. This treatment was first worked out by me in dogs and published in hunting and fishing magazines. Several physicians have cured rattlesnake bites using this treatment schedule; their voluntary letters are in my files.) The vitamin must be given by needle in massive doses and around the clock to obtain these results.

Intravenous TOLSEROL, given in adequate amounts, has no equal in controlling the convulsive seizures found in tetanus. In our case of the six-year-old boy weighing 20 Kg. we gave as an initial dose 200 mg of Tolserol in 500 cc of D5 water at a rate of 35 drops per minute. Since no dose schedule was available for children at that time (September 1951), we experimented with this amount since we did not desire too great a relaxation. Prostigmin was made available for this emergency. There was no response to this amount of Tolserol, so after six hours an additional 800 mgm was given, using the same type of diluent. The results obtained proved that this was the drug of choice in producing relaxation and preventing convulsive seizures in tetanus. This fact was apparent before the fluid run was completed. Subsequent doses of Tolserol were set at 1000 mgm. This amount gave complete control of all muscle spasm for a period of 60 hours. Under the influence of intravenous Tolserol the patient immediately began to take nourishment by mouth, was not disturbed by noises in excess of what should be expected in a hospital and did not require a darkened room. Nursing care was limited to that given by "floor nurses," although we did keep a companion in the room at all times as a psychological measure. The same day that intravenous Tolserol was given the patient played with toys in his bed and used crayons to color pictures in a color book. After about 60 hours this interest was suddenly lost and mild spasms returned. This pattern was just as suddenly reversed by giving another 1000 mgm of Tolserol intravenously. Other types of therapy were employed in this case. A review of his hospital course will argue the case for vitamin C and intravenous Tolserol. At only one period

of his hospitalization was the outcome in doubt and this was due to a reaction to serum. Here again Tolserol and vitamin C saved the day.

He was admitted 9/1/51 at 30 minutes past noon. Two grams Vitamin C were given intravenously at 1:00 p.m. Liquids taken freely throughout afternoon. 6:00 p.m. 2 grams of vitamin C. (All vitamin C and Tolserol given in this case was administered intravenously.) At 8:15 p.m. child reported crying loudly. A.S.A. grains V given by mouth with some difficulty. 9:00 p.m. 2 grams of vitamin C. At 10:40 p.m. an S.S. enema was given with good results. The procedure did not excite muscle spasm. 12:00 midnight 4 grams of vitamin C and one 10 cc ampule calcium gluconate. Child sleeping. At 3:00 a.m. 4 grams vitamin C. Patient having moderate abdominal cramps; no difficulty in swallowing. 6:00 a.m. condition same; given 4 grams vitamin C. 8:00 a.m. some difficulty in swallowing; 4 grams vitamin C given at 9:00 a.m. and by 10:00 a.m. was resting quietly. Sleeping at 11:00 a.m. and at 12:00 noon voided 100 cc urine. (From this point kidney output was normal.) Taking fluids freely by mouth. At 1:00 p.m. 4 grams vitamin C and 600,000 units procaine penicillin. The entire afternoon was spent "lying quietly" in bed. Fluids now protinal in milk and egg in milk; no difficulty in swallowing. At 6:00 p.m. and 9:00 p.m. 4 grams of vitamin C. Nembutal suppository grains 2 ordered by intern but there was no restlessness. The explanation for this order was "so the boy would get off early to sleep." At 12:00 midnight was given aspirin grains V, 4 grams of vitamin C and 600,000 units procaine penicillin. The rationale of the penicillin was to prevent secondary pulmonary pathology. The night of September 3rd was uneventful; he received 4 grams of vitamin C at 3:00 a.m. and at 6:00 a.m. Had mild abdominal cramps, off and on, through the morning. At 10:00 a.m. 4 grams of Vitamin C; sleeping at intervals. Because of "outside pressure" 25,000 units TAT were given with saline intravenously, after skin testing for sensitivity. This was at 12 noon. By 1:00 p.m. his temperature was up to 101° F. rectally, the highest since admission; refused egg in milk. 2:00 p.m. voided 300 cc urine. At 3:00 p.m. he was crying because of severe pain in his abdomen. Floor nurse reported in her daily log—"an uncom-

fortable period since antitoxin." 4:00 p.m. 4 grams vitamin C, refused all liquids but by 5:00 p.m. was sleeping. Since antitoxin therapy was not our decision we elected to be heroic and give it a test to prove its lack of value.

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Tri-State Medical Journal

Published Monthly by the
TRI-STATE MEDICAL ASSOCIATION
with offices at 122 S. Greene St.,
Greensboro, N. C.
R. B. DAVIS, M.D., *Editor*

VOLUME II

JULY 1954

NUMBER 5

CONTENTS

President's Message.....	<i>Fred Kredel</i>	5
Editorial—Is It Becoming a Habit?	<i>R. B. Davis</i>	6
Recent Discoveries in the Treatment of		
Lockjaw with Vitamin C and Tolserol	<i>Fred C. Klenner</i>	7
Venom Poisoning.....	<i>Leon J. Taubenhaus</i>	12

Dr. Fred Klenner briefly reviews the physiology and environment of black widow spiders and discusses the diagnosis and treatment of their bites. There is wide variability in severity of bites. He recommends 350 mg of ascorbic acid per Kg of body weight administered intravenously along with a single dose of calcium gluconate by needle as the method of choice. He is critical of physicians “who would stand by and see their patients *die* rather than use ascorbic acid—because in their finite minds it exists only as a vitamin.”—*R.D.M.*

The Black Widow Spider: Case History

Fred R. Klenner, B.S., M.S., M.D., F.C.C.P., Reidsville, N.C.

Tri-State Medical Journal, December 1957, Vol. 5, No. 10, pp. 15–18

The Black Widow spider has a wide distribution, extending from Canada to southernmost South America, the Hawaiian Islands, the Bahamas and West Indies. She produces, on the average, five egg sacs each season, yielding over one thousand spiderlings. Except for man, she has only one real enemy, the parasitic fly, *pseudogaurax signata* (Loew). This tiny fly lays its eggs on the spider's egg sac, where, after two to three days, they hatch. The larva then “worm” their way through the fabric of the egg sac and devour the eggs of the Black Widow. The maggots, after their *concentrated diet*, proceed to pupate in the Widow's nursery. In a few weeks the cocoons burst and the adult “Gaurax araneae” flies emerge, gnawing through the Black Widow's sac, only to seek out and destroy others. This female spider is extremely temperamental, not only in what “insects” she bites but also in her romance during her mating activities. Once a timid male finds her receptive to his advances she, very often, after satisfying her sexual impulse, will kill her insatiable little husband— hence the name Black Widow.

Spider lore, legend, facts. Books could be written covering these aspects. This paper will deal only with *facts*.

Some spider-bite victims escape without any ill effects, others suffer mildly, while still others experience excruciating pains, and, in some instances, death. The Black Widow, like other spiders, is equipped with a pair of fangs. The “Widow” differs from other spiders in that her fangs are fed by unusually large poison sacs. These sacs are not glandular, as we usually interpret its meaning, but function as absorptive organs which take up the poisonous constituents from the body fluid of the spider. The chemical and physical properties of the poison indicate it to be a neurotoxin, probably a toxalbumin, possibly a poisonous enzyme. The toxicity is destroyed by heating to 159 degrees F. for 45 minutes. It cannot be crystallized since desiccation destroys it. It has been preserved in glycerine for several months. The fangs project from the head of the spider, the points curving towards each other. On the convex sides, at their tip ends, there are tiny openings, and these apertures emit the poison when the sharp points

pierce the skin. The fangs are so positioned that it is impossible for them to be closed by the pressure created by the bite. The poison glands are situated in the head-part of the spider, and are enclosed in a very fine, membrane-like sac, which can be extracted with the fangs in a careful dissection. Each fang has its own individual poison pouch. These pouches (or sacs) are surrounded by a series of striated muscles, and compression of the sacs by these muscles causes the venom to be discharged. These muscles operate ONLY at the *volition* of the spider. The Black Widow may strike one person without injecting any poison into the wound, and in another instance, only a small amount; in still another case, the maximum contained in a single sac, and in yet another a portion approximating the full content of her venom sacs. It must also be remembered that should the spider contact a human subject shortly after she has expended her venom in subjugating an insect, the bite will be harmless, or certainly no more toxic than the bite of any one of a dozen less important spiders or insects. The age of the spider, her physical condition, whether or not she has recently fed, her temperament (for on being disturbed she might "play dead"), the area of the bite, for if the strike occurs where the skin is thick the fangs might not even break through, and the *all important* factor of the age and physical condition of her human victim will also determine the seriousness of the bite. The toxin of the Black Widow has a QUANTITATIVE effect; thus a given quantity would tend to be more serious in a child than to an adult. Certain individuals may be allergic to the poison, while others may have an uncommon type of resistance. One should always remember that the Black Widow spider could have, and this is a FACT proven, a venom supply at her command sufficient to cause intense suffering in any human subject and that it is always possible for a series of conditions to exist whereby DEATH to the victim will ensue.

DIAGNOSIS

Arriving at a correct diagnosis in Black Widow spider bite is of cardinal importance. The severe bite "mimics" many other serious pathological conditions; namely acute pancreatitis, biliary or renal colic, food poisoning, lock-jaw, angina pectoris, volvulus, coronary thrombosis, diffuse peritonitis, intussusception, lobar pneumonia, perforated gastric or duodenal ulcer and strangulated umbilical hernia. In our case the parents interpreted the child's illness, initially, as *food poisoning* and later as *intestinal obstruction*. In a typical case of a person who is bitten, say, upon the palm of the hand, the pain will progress upward to the elbow, from thence to the shoulder area, and then down the trunk of the body toward the region of the kidneys, following which the abdomen becomes rigid. Other various symptoms are: cold perspiration, an increase in the blood pressure (thus a bite in a patient with existing hypertension might prove fatal by the indirect route of cerebral hemorrhage), a rise in body temperature (the higher the fever curve the greater the danger for a fatal termination to the bite), nausea and anorexia, vomiting, slight twitching or spasms of the muscles of the extremities, malaise, urinary retention, constipation, speech defect, local oedema, difficult breathing, restlessness, cynosis, vertigo, chills, paralysis, a macular skin eruption, convulsion, prostration and delirium.

The aforesaid symptoms represent three significant phases: (1) The rapidity with which the poison is distributed throughout the body. Thus the initial effect presents

itself early, the interval between the bite and the first symptom, which is pain, being sometimes a matter of only a few minutes. (2) The degree of pain experienced in various parts of the body. Usually there are cramps and spasms in all of the larger muscles of the body. The pain can be so excruciating that numerous accounts record that the spider-bite victims roll and toss and moan in agony upon their beds of pain. (3) The many GENUINE cases of Black Widow spider bite have been wrongly diagnosed. Fortunately a GOOD HISTORY *plus* a few simple laboratory tests will allow a proper evaluation. A knowledge of the fang marks can, alone, make the diagnosis. The advice of Ginsburg is worth reviewing: "In the case of ruptured ulcer versus Black Widow bite a history of a BITE will be elicited, no history of ulcer symptoms, course of spread from bitten area to abdomen, mild or no collapse, temperature normal or slightly elevated, pulse slightly faster, cramp of extremities, X-ray negative for gas bubble, and the patient can sit up or move about. A ruptured ulcer gives no history of a bite, history of ulcer symptoms, knife-like pain at the point of rupture, collapse, temperature subnormal, no cramps of extremities, X-ray evidence of gas bubble in majority of cases, and the patient remains very quiet—does not want to be moved."

TREATMENT

Bogen, Thorp and Woodson state that more than NINETY different remedies have been employed in the treatment of the bite of the Black Widow. Since the introduction by Stewart and Gilbert of the intravenous use of calcium chloride or calcium gluconate, all other therapeutic measures are of "academic" importance only. In 1925 Bogen did use human convalescent serum, and at that time reported "that although theoretically sound and of unquestioned value, nevertheless the results were NOT so striking as to 'make it the most valuable treatment.' " Later he, Bogen, stated that calcium gluconate proved so effective that the use of serum was seldom indicated. Still later, however, a new serum, traded named "Lyovac" antivenom was introduced. This serum is dehydrated by a special process of rapid freezing and dehydration under high vacuum, called lyophilization. Since there is an element of risk with the use of this serum it must NEVER be used until a negative intradermal skin test and eye test have been obtained. It cannot be denied that serious sickness and even death can result from its use. The usual dose is 2.5 c.c. given by the intramuscular route, preferably the deltoid muscle. Our purpose in this paper is to introduce a NEW treatment to cure the bite of the Black Widow. Ascorbic acid in the amount of 350 mg. per Kg. body weight given intravenously in conjunction with a single dose of Calcium gluconate is suggested as the treatment of choice.

CASE HISTORY

White female 3½ years of age, suddenly became ill while at play on a pile of old bricks. She refused supper, complaining of severe griping pain in her abdomen. A series of trips to the "bathroom" were non-compensating. Nausea was present most of time and this was followed by vomiting some six hours after onset. The vomiting continued, off and on, throughout the night. The illness was interpreted as a food intoxication by the child's parents. The following morning, roughly 12 hours from onset of illness, she

had $1\frac{1}{2}$ degrees of fever, and was very moody. As the fever continued to rise, the mother observed a redness about the child's umbilicus associated with considerable swelling and rigidity. The slightest pressure elicited severe pain. Over the next several hours the child's condition progressively became worse. The speech became incoherent and shortly thereafter the child became increasingly stuporous. At this point the mother of the child called my office and reported that because of the pathology described in the area around the umbilicus, she felt that a condition of obstruction existed. There had been no bowel movement since the preceding day. She was instructed to bring the child for examination. At 10 a.m., approximately 18 hours after onset, the situation was this: A young female lying prostrated on the examining table. The child made no response, verbal or physical, to questions asked. The fever was recorded at 103.5 F. Axillary 5 minutes (corrected). The area around the umbilicus, about the size of a man's palm of his hand, was indurated, dark red in color, warm to touch and in the very center the protrusion resembled a hernia under pressure. On close inspection, however, two tiny spots, about $\frac{1}{8}$ inch apart, were observed within this edematous circle. With the aid of a magnifying glass it became obvious that these were the fang marks of the Black Widow. The breathing was now labored; the abdomen was boardlike. I suggested to the mother that this was a case of a Black Widow bite, but she was not impressed, since there was no history of a bite. I was so positive of the diagnosis that I informed the mother that I would treat the child for that particular pathology. Ten c.c. of calcium gluconate was immediately given intravenously. This was followed within 15 minutes with four grams of ascorbic acid, also given intravenously. Although the child was critically ill, I was so confident of the success of the treatment that when the Father requested to take the child home rather than to the hospital, I agreed. Seen six hours later, she was responsive to manipulations, especially pressure on the abdomen. The fever curve was down to 101 F. Axillary 5 minutes (corrected). Nothing by mouth had been attempted. Four grams of ascorbic acid was given intravenously and the child again allowed to go home. Instructions were given to try water by mouth and if and when successful to switch to strained orange juice and coca cola. The child was again seen in six hours, that time at her home. She was listless but awake and taking fluids in small amounts without difficulty. The fever curve was now at 100 F. (A) Corrected. Instructions were given for the night, which was uneventful, and the little patient was again seen around 10 a.m., the following morning, in the office. Now she was awake, relatively active, not so tender and about 50 per cent of the swelling and discoloration about the umbilicus gone. She was given four grams ascorbic acid intravenously and three grams intramuscularly and allowed to return home. The next three days showed continuing improvement, ascorbic acid 1000 mg. by mouth every 3 to 4 hours was the only medication; her diet remained liquid to semi-soft. On the fourth day it was made known that the child had had no bowel movement since the day of the bite. The mother was instructed to give an oil retention enema and if this failed, to follow in two hours with a fleets enema. A large TAR-LIKE stool was passed following the "fleets." This finding was previously reported by Herms and others "AT AUTOPSY"; to wit: "Post mortem examinations showed the stomach wall ruptured and the small intestine filled with a bloody fluid." Following the bowel movement the child's appetite immediately improved and her return to normal

was rapid and uneventful. Following her recovery the child told of “knocking a big black bug off her stomach” the day of the bite.

CONCLUSION

The Black Widow (*Lactrodectus mactans*) inhabits your back yard, or if not yours, then certainly that of your neighbor. There exists, then, a potential danger to all of us. A rock, a brick, or an old board should not be raised without taking every precaution, unless thick canvas or leather gloves are worn. Such activities must never be practiced after dark. One should always lift an object from the ground with the expectation of finding a Black Widow. Your eyes might first see a bright, shiny, black ball. If this “ball” is touched, gently, with a small twig, the full spider will reveal herself. Outdoor privies are common “hang-out” places; so are the openings in cinder blocks. I have killed three mature “Widows” in the back corner of the brick alcove entrance to our home. A pair of shoes allowed to remain on the porch is a likely spot, for she likes dark recesses. The bite of the Black Widow can “mimic” many serious pathological conditions; always consider this possibility in your differential diagnosis. The attack of KIDNEY COLIC which started in the garden, might well be, in reality, the BITE of the Black Widow. The usual symptoms following the bite of the “Widow” are rather well marked, yet to the practitioner not familiar with them they are as if none exist. This is one of the reasons for writing this paper. I have treated eight proven cases of Black Widow bite during my tenure as a physician; I have actually seen no more “bonified” cases of RENAL COLIC. The treatment of the bite is very important. It is criminal to give these patients an opiate to relieve their pain, for in so doing you might add to their distress and actually precipitate a fatality. This is not a prophesy; honest physicians have reported case histories on such “accidents.” It is never necessary to subjugate these patients to a variety of therapeutic measures, such as tepid baths, for such must be recognized as not intended for the benefit of the “victim” but only for his family, friends and relatives. If your choice of treatment rests with ANTIVENOM, then you might be forced also to employ other “foolish” practices. Calcium gluconate, alone, has CURED many, many cases of the Black Widow bite. In my hands it has done just this, and done it well, although in three instances two and in a third case three injections were required. In the case we have presented here, I doubt, if even the skeptic would question the serious nature of the bite. Yet only one dose of calcium gluconate was given. Since ascorbic acid behaves much like calcium in the body, and also acts synergistically with it, we elected to observe its action. The fact that the child recovered, even without supportive therapy, will argue the cause for us. This child, according to the rules, should have died. She lives, in our opinion, because we elected to use this powerful therapeutic agent. But, then, there are some physicians who would stand by and see their patient *die* rather than use ascorbic acid—because in their finite minds it exists only as a vitamin.

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In this article published in 1957, Dr. Fred Klenner describes successfully treating a nineteen-month-old child suffering from what he described as a “brain pathology caused by an insidious virus.” “After fourteen years of research,” he says, “we are convinced that ascorbic acid is the drug of choice in virus pathology.” “We are convinced,” he goes on to say, “that it should be a *maxim* of medicine for large doses of ascorbic acid to be given in all pathological states. It should be given by all physicians while they wait their diagnosis.” Mystified at the lack of acceptance of his research findings, he adds, “The information which we have published on the use of ascorbic acid since 1948 makes me wonder what the response might have been had the source of reporting been a large teaching unit of a major research center.”—*R.D.M.*

An ‘Insidious’ Virus

Fred R. Klenner, B.S., M.S., M.D., F.C.C.P., Reidsville, N.C.
Tri-State Medical Journal, June 1957, Vol. 5, No. 4, pp. 10–12

“**E**verything that is written in books is worth much less than the experience of one physician who *reflects* and *reasons*.” So wrote *Rbazes* who lived 850–923 A.D.

February 5th, 1950, while on emergency call at the local hospital, we saw a white baby, 19 months old, who according to its mother, was bothered with a little cold for two weeks. Twenty-four hours prior to hospital admission, this child began “running a high fever that could not be broken with aspirin.” Clonic convulsive seizures of the right arm and leg began 12 hours before coming to the hospital. The presenting picture was that of an undernourished infant, lying rigidly in its mother’s arms. The skin was cold to the touch, color actually ‘cadaver-like,’ eyes closed. There was a grade II mucopurelant nasal discharge and the throat, difficult to visualize, was red. The rectal temperature, which tended to confuse the picture, was 98.4 °F (uncorrected). Areas of skin over the back presented an appearance similar to that seen in rigor mortis. Two grams ascorbic acid was given intramuscularly while the child was in the emergency room and one gram was given approximately 45 minutes later on the ‘floor.’ Following the second injection, ascorbic acid was given every four hours, one gram each time. It was more than academic interest to note that the child *did not* respond to pain with the initial injection of ascorbic acid. To give rapid external heat, mustard plasters were applied to the anterior and posterior chest, the plasters being preceded by an application of olive oil. The proportions used in preparing the plasters was one part mustard to three parts flour and cold tap water was employed in making the paste. A croup tent was set up using bathe blankets which were fastened to the ‘crib’ bed with large safety pins. The steam vapor carried compound tincture benzoin. 50 c.c. 5D in saline was given under

the skin in the scapular areas. Two hours following the first injection of ascorbic acid our little patient drank 240 c.c. of orange juice from a bottle which was held by a nurse. This was the first nourishment, even water, taken by the child in 24 hours. The baby, at this point, was beginning to respond to pain. The same amount of orange juice was repeated 1½ hours following the completion of the first bottle. The temperature, at this point, was 103.8 °F rectally (uncorrected). Roughly four hours following admission to the hospital it was possible to determine that this little patient had a complete paralysis of the right arm and leg. It was pathetic to observe the quickened, purposeless movements of the left extremities. Eight hours later, however, the right leg was moved and one hour beyond this time, by the clock, the baby grasped a bottle of orange juice with both hands. From this point on the recovery was un-eventful. Penicillin (single injection type) 200,000 U was given on the 2nd and 3rd hospital days to *discourage secondary* invaders. The patient was discharged on the 5th hospital day.

Since 1950, at least six additional cases, presenting a similar picture, have been admitted to Annie Penn Memorial Hospital, Reidsville, North Carolina. The difference 'in results' suggested the preparation of this paper. All six children were under four years of age. Four of these cases were seen by the same physician and in each instance his remark at case conference was that he was "not impressed with the illness of the child." The significant finding as reported by this doctor was that no fever was recorded. All four children were dead within 30 minutes to two hours following the initial examination. No treatment was started because in the words of the attending physician no diagnosis had been established and that he was opposed to administering medication without knowing the pathology. We will not debate the merit of this opinion. We remember, however, an old, old story which related how a Kingdom was lost for want, in the first place, of a 'nail.' An autopsy was performed on one of these patients. Pathology, as reported, was limited to the chest which showed bilateral involvement of the bronchial tree compatible with a virus infection. (From our own observation in two cases we believe that this child, as well as the others, died from an insidious virus involvement of the brain.) A fifth case was seen by two other physicians. They, too, did not arrive at a diagnosis and therefore withheld treatment. When, on the second hospital day, the patient demonstrated convulsive seizures a spinal tap was done with the fluid being reported as within normal limits. The child died on the 3rd hospital day *without* treatment. One explanation advanced at case conference was that they were awaiting the return to town of a third consultant and the second was that they, too, did not believe in treating a disease before the diagnosis had been established. Life is a continual battle between error and truth, but as Balzac wrote: "Opinions are caught like an infection, and put into practice without examination."

It was Lamartine who said: "Chance often gives us that which we should not have presumed to ask." The sixth case was mine on Monday, April 5th, 1957. This was a well developed, well nourished eighteen month old white female who was brought to my home about 7 p.m. by the child's Uncle and Aunt. The history was brief. The child had strangled on food while eating supper and it appeared to them that she would not recover. A cursory examination given in the front seat of an automobile revealed an extremely restless, whining child. The temperature, taken five minutes axillary, was 98.6 °F (cor-

rected). There was no obstruction to the air-ways. These findings were not compatible with the history. Finally, we elicited the information that the patient had had a cold for the past several days. We also learned that the child's mother had taken it for a long stroller ride the previous day—which in this area was damp and windy. Frankly, the impulse to send the child home without treatment was great. Remembering the cases described in this paper, we elected to 'buy' some time. The Uncle was asked to take the child to the emergency room of the local hospital, where, he was assured, a nurse would be instructed to give it an enema. The nurse on duty was asked, by phone, to take a rectal temperature and then give a fleets enema. If the results proved un-satisfactory she was to repeat the procedure in thirty minutes using a normal saline solution. Approximately forty-five minutes after leaving my home the intern on duty reported to me, by phone, that the child was 'out' and responded only to pain. The enema had not been given. Going at once to the hospital we found conditions exactly as described. The little patient was lying motionless on the examining table. Response was elicited only to pain. Using a suitable size rectal tube I, myself, gave the enema with good results. The stool was normal. The rectal temperature taken at the hospital was 98.4 °F (corrected). Associated with this was a pulse rate of 159 per minute and respirations 32 per minute. It was impossible to visualize the throat because the mouth was 'locked,' as one finds, after stimulation, in lockjaw. Repeated attempts to view the throat resulted in the child assuming a position of opisthotonos. Our impression was an 'insidious' virus infection. After fourteen years of research we are convinced that ascorbic acid is the drug of choice in virus pathology. Accordingly 2½ grams was given intramuscularly in the emergency room and two additional grams ascorbic acid was given approximately 30 minutes later on the 'floor.' Following this ascorbic acid was given every 2 hours for 5 doses then changed to q.4.h. After 36 hours ascorbic acid was extended to every 6 hours and eighteen hours later cut to one-half gram every 12 hours. Thirty grams ascorbic acid was given in all. A croup tent using bathe blankets was set up, the primary purpose being to keep a draft off the patient with the opening and closing of the room door. Steam vapor carried menthol. An adult hospital type woolen blanket was quartered and tucked around the child. Crystalline penicillin, 25,000 U, was given intramuscularly to destroy secondary invaders and this was repeated in one hour, then every two hours for 4 doses and subsequently at four hour intervals for 48 hours. This method of administering penicillin was adopted to compare with the single sustained dose type used in the case treated in 1950.

One hour following admission we applied a 4 x 4 gauze, saturated with water, to the child's lips. The sucking reflex was still intact, but the child immediately strangled. Turning the child quickly head down, the small amount of water taken ran from its nostrils. Now it was clear. It was this 'bulbar phenomenon' that was at play while the child ate its supper. The nursing log showed the temperature to be 99 °F rectally (corrected) one and one-half hours after admission, and one and one-half hours later was up to 100 °F. The nursing log at this point read: "Shows no sign of consciousness." Temperature 101.2 °F at four hours and up to 102 °F after five hours. By 2 a.m. (6 hours following admission) the fever curve had climbed to 102.4 °F and now the nursing log read: "Baby swallowed water without difficulty." Following this the temperature curve started back down and by 7 a.m. (11 hours following admission) the child was alert

and taking water freely from a spoon. Twenty-four hours after the first injection of ascorbic acid the temperature was back to 99.0 °F and four hours later was normal. Water, milk and orange juice were now taken from a bottle. Terramycin pediatric was started 6 hours after admission but was discontinued after the fifth dose due to diarrhea. This was corrected with lacinex granules. The child was discharged on the 5th hospital day.

CONCLUSION

It is reasonable to believe that had this child been put to bed following her evening meal episode, that she would have *died*, that night, while in her bed. Most likely, then, the cause of death would have been recorded as suffocation or perhaps strangulation by way of regurgitated food. The *real* cause of death would have been *brain pathology caused by an insidious virus*. Every practicing physician can, possibly, recall a similar situation as described in this paper. To indicate just how common this condition really is a case history of a 15 year old girl, living in a near by town, is cited. This girl had a mild, lingering cold for several weeks. Attended a dance party one evening and except for a complaint of feeling extremely tired went to bed *apparently* well. She was found *dead* in bed the following morning. An autopsy showed bi-lateral virus pneumonia. What was not reported and what was most likely the actual cause of death was a virus inflammation of the brain by 'an insidious virus.' These cases are suggestive that the toxins of this particular virus act like a 'cephalic tetanus-toxemia.' The motor nuclei which have the shortest motor nerves are reached earliest and it would seem then that this condition may culminate in diaphragmatic spasm, with dyspnoea and even *asphyxia*. Many who are dying—don't have to die. Ascorbic acid, in proper doses, first by needle and later by mouth, can and will save countless individuals once physicians awaken to the real value of this drug. Ascorbic acid, however, is not a panacea. Not all cases will recover, because once the pathological process has progressed to a certain unknown point, it cannot be reversed. The detailed case histories here presented give us an index. We are convinced that it should be a *maxim* of medicine for large doses of ascorbic acid to be given in all pathological states. It should be given by all physicians while they wait their diagnosis. These large doses should not be continued once the temperature curve approaches normal. False temperature spiking will result. We have, more recently, observed in other virus cases to be reported later, that doses of 400 mg. per Kg. body weight given with three to seven hundred c.c. 5% dextrose in water and also containing 250 to 500 mg. achromycin or panmycin will bring about 12 to 24 hour cures which are not 'touched' by any other combination of antibiotics. We have further observed that ascorbic acid taken from ampules and mixed with orange juice and taken by mouth give just as good results as the injections. Where veins are difficult to find and the patient cannot swallow then the mixture can be placed into the stomach by way of a tube. This report argues the importance for physicians to always compare the case they are treating with similar cases seen in the past. This led someone, long ago, to say: "The longer one practices the more he knows what to practice." The information which we have published on the use of ascorbic acid since 1948 makes me wonder what the

response might have been had the source of reporting been a large teaching unit of a major research center. There is no doubt but that physicians are being 'brain washed' with the current journal advertizing. Herbert Spencer summed it up rather well: "There is a principle which is a bar against all information, which is proof against all argument, and which cannot fail to keep a man in everlasting ignorance. That principle is condemnation without investigation."

Note from the Editor: The original article included no bibliography.

Dr. Fred Klenner presents case histories on the insidious virus disease he described in his June 1957 article in the *Tri-State Medical Journal*, reprinted here. He presents recommended intravenous vitamin C dose levels and suggests a treatment schedule in some detail. He notes the preferred degree of dilution of the vitamin when the needle is used. He also describes a simple method to assess urine levels of ascorbic acid.—*R.D.M.*

The Clinical Evaluation and Treatment of a Deadly Syndrome Caused by an Insidious Virus

Dr. Frederick R. Klenner, Reidsville, N.C.

Tri-State Medical Journal, October 1958, Vol. 6, No. 8, pp. 11–15

“**E**very human soul leaves its port with sealed orders. These may be opened earlier or later on its voyage, but until they are opened no one can tell what is to be his course or to what harbor he is bound.”¹ All too often the individual has been *discharged* without knowing the contents of these orders.

In June, 1957, I was privileged to have published in the *Tri-State Medical Journal* a paper on “An Insidious Virus.”² Additional cases of my own, in adults as well as in children, along with similar “Case Histories” reported in the *obituaries* of several newspapers, seemed evidence enough for this second report.

Two important stages are recognized in this deadly syndrome: Stage (A)—(1) There is a history of having had “the flu” which lasted forty-eight to ninety-six hours, complicated by extreme physical or mental stress; (2) a mild cold, similar to an allergic rhinitis, which lingered on for several weeks but did not incapacitate the individual. Stage (B)—This stage, which is always sudden, will present itself in at least six forms: (1) convulsive seizure; (2) extreme excitability resembling delirium tremens if an adult and with *dancing* of the eyeballs if a child; (3) severe chill; (4) strangling in the course of normal eating or drinking; (5) collapse; (6) stupor.

Other findings of this dramatic second stage are (1) rapid pulse; (2) the temperature can be normal or moderately elevated; (3) respirations twice normal and in some cases will be suggestive of “air hunger”; (4) the pupils in our cases have been dilated with one pupil slightly wider than the other; (5) the urine negative; (6) the white blood count elevated, running from 9,000 to 35,000; (7) in young patients starting the second phase with a convulsion there has been not only a history of normal bowel movements but an enema given at the time of first examination has also been normal; (8) bladder spincter control was abnormal in our cases who convulsed or were in coma when first seen.

It is apparent that the second stage of this syndrome is “triggered” by a *break-through* at the site of the choroid plexus. The time required for neurological changes to

become evident following this passage of the virus and/or its toxins across the "choroid barrier" is roughly comparable to the time necessary for similar neuropathology to be demonstrated following a severe head injury. Cerebral edema certainly exists in both conditions. Although the cause differs, one mechanical the other chemical, the effect is the same. In this situation, however, one usually has the advantage of knowing whether or not trauma is the causative factor. Differentiating between a virus encephalitis and some other type of space consuming lesion of the brain can precipitate a time factor with a margin of safety so narrow that life and death is separated *only* by minutes. In this emergency the attending physician cannot and must not wait for laboratory procedures.

Case History no. 1: 64-year-old white female was seen at 1 P.M. for a routine check of her blood pressure prior to taking a trip. She gave a history of having had a slight cold which lasted for a few days, roughly one week, prior to this examination. On this visit the temperature was normal as were other findings including her blood pressure. She then departed for a visit with a friend, 150 miles from her home. At 10 P.M. the same day I was called by the patient's husband who reported that his wife became ill, suddenly, after arriving at their planned destination and that they had returned home. A few suggestions for therapy were given by phone with the added understanding that the husband would report on his wife's condition at a later hour. Called again at 1 A.M. the following day, which was just 12 hours from the time of the original routine examination, I found the patient in coma with a temperature of 104° F. (A) She was removed by ambulance to the local hospital. On admission her temperature was recorded at 105° F (Ax. corrected), pulse 120 and respirations 24. Achromycin 500 mg. and ascorbic acid 26 grams were added to 375 c.c. 5% dextrose in water and given intravenously with a drop rate of 75 per minute. The patient was also given nasal oxygen running 5 liters per minute. Consciousness returned one hour following admission; the patient, however, could not swallow water when offered. She was incontinent. The fever dropped to 102.6° F (Ax. corrected) by 11 A.M. but by 12 noon (9 hours following admission) was back up to 104° F. Achromycin 500 mg, and ascorbic acid 26 grams in 375 c.c. 5D water was repeated. Respirations at this point were 36 per minute. Achromycin 500 mg and ascorbic acid 16 grams was given at 11 P.M. By midnight the temperature was 100° F. (rectal) pulse 84 and respirations 28. By 12 noon of the second day (36 hours following admission) the patient's ability to swallow suddenly returned. Following this episode the convalescence was uneventful. Temperature, pulse and respirations remained normal. Achromycin 250 mg. and ascorbic acid 4 grams were given by mouth every four hours. She returned home on the third hospital day. The admission white blood count was 18,000.

Case History no. 2: Five-year-old colored male was seen in my office because the child had had a convulsion 24 hours earlier. The temperature was 104° F (rectal), pulse 130 and respirations 18. The child was extremely restless. Physical examination was within normal limits except for the throat which was red and the turbinates which were swollen. While in the process of writing prescriptions, the child experienced a

second convulsive seizure. Following the convulsion four grams ascorbic acid was given intravenously and the little patient sent on to the hospital. On admission three grams ascorbic acid was given intramuscularly and this was followed with four grams in a glass of orange juice every four hours. Chloromycetin palmitate, one teaspoonful, was given every four hours. The hospital course was actually uneventful as the fever curve broke sharply and was normal in 12 hours. He was discharged after one hospital day to continue the above medication for a period of three days. His white blood count on admission was 9,350.

Case History no. 3: Sixteen-months-old white male was given treatment for a mild cold two weeks prior to admission. On the day of admission child seemed normal in all respects, accompanied his parents to church services and then was taken to a friend's house for refreshments. While at the neighbor's home the child suddenly collapsed while standing by a chair and immediately was unconscious. Seen in the emergency room of the local hospital the child lay prostrated on the examining table. The pulse was too fast to count and the child's respirations were above 40 per minute. The eyes were red and "wet." The temperature was 103° F (R). Nasal oxygen was started and two grams ascorbic acid was given intramuscularly. The child was conscious within 10 minutes. He was then removed to a hospital room where two additional grams of ascorbic acid was given, also by needle. This drug was continued every two hours for five doses then extended to four-hour intervals for twelve times. Achromycin drops (50 mg. each dose) were given every four hours. The physical examination and laboratory studies indicated that the child also had bilateral pneumonitis. The temperature was normal after sixty hours. The fever spiked to 102° F (R) on the fourth day and returned to normal following subcutaneous fluids. He was discharged on the seventh hospital day. White blood count on admission was 10,300.

Case History no. 4: 2½-year-old white male seen in my office for examination due to a lingering cold of 10 days duration. Temperature 101° F, throat red, tonsils slightly enlarged, turbinates swollen with grade I mucoid discharge. The ears were negative and the chest was normal to auscultation. Heart normal but the pulse was 130. The eyes were red and "wet." Respirations were labored and fast; this was attributed to his nasal congestion. Prescriptions were written and the child allowed to return home. Fifteen minutes after leaving my office and while the child's mother was having the prescriptions filled the child suddenly began a convulsive seizure. The father returned the child to my office, still convulsing. Three grams ascorbic acid were given intramuscularly; the child did not respond to the pain of this injection. The temperature was now 103° F. The pulse was extremely fast as were the respirations. The child was unconscious. Oxygen was administered from a portable cylinder using a rubber face mask and after roughly 10 minutes the breathing returned to that similar to normal sleep. At this point he was taken to the local hospital. On admission he was given two additional grams ascorbic acid intramuscularly and this was repeated in one hour and then every two hours for 4 doses and finally every four hours for 4 doses. Crystalline penicillin, 25,000 units, was given intramuscularly six hours following admission to

guard against secondary invaders. The temperature at this time was 100° F (R). The penicillin was repeated after one hour and then given every six hours. Terramycin pediatric, 25 mg., was also started and given every six hours. The temperature was recorded at 104° F (R) on admission and was normal nine hours later and remained so for the duration of the hospital stay. It is also interesting to note that the "nursing log" read "sleeping" on several hourly notations following admission and after five hours read "taken and retained fluids, respirations slower," and nine hours following admission read "taken milk as if starved." He was discharged on the second hospital day.

Case History no. 5: This case is presented to demonstrate quick response to therapy and also what can happen if treatment is discontinued too soon. This patient had three hospital admissions within 24 days. The pathology was the same on each admission. The patient was a 73-year-old white male. Entered hospital by way of ambulance in an unconscious state. His family gave the history that he had had a slight cold for 10 days prior to his present illness which started with a severe headache, was followed after several hours with a chill, and this was followed one hour later with sudden unconsciousness. On admission his temperature was 103° F. (R), pulse 138, respirations 36, B.P. 150/90. He did not respond to stimuli. Moist rales were heard over the main bronchial tree. The heart was enlarged to the left; otherwise not remarkable. Under-nourishment was marked. Shortly following admission he experienced waves of myoclonic jerks involving all of the skeletal muscles. This prevailed for several hours, and an impression of "progressive cerebral degeneration" was entertained. He was started on nasal oxygen running at 5 liters per minute. Metrazol 0.1 gram was given intramuscularly and this was repeated every eight hours. Achromycin 500 mg and ascorbic acid 20 grams was added to 375 c.c. of 5% dextrose in water and given intravenously; this was repeated in eight hours. Suction and atropine 1/100 grain, given intramuscularly, was employed for bronchial secretions. He regained consciousness 18 hours following admission. Dilantine sodium 0.1 gram was given one hour before meals and at bed hour. The admission white blood count was 10,000. The urine was negative. He was discharged, apparently well, on the third hospital day. He was re-admitted to the hospital 14 days later with the same findings, was given the same treatment and was discharged on the fourth hospital day. The white blood count on this admission was 18,850 with 82% segmented. He was re-admitted to the hospital seven days later with the same findings, except that on this occasion he was conscious. The same treatment was employed except that 24 grams ascorbic acid was used in place of the earlier 20 grams. His white blood count on this admission was 35,900. He was discharged on the third hospital day. This time he was given a 'holding dose' of achromycin V 250 mg. with citric acid (one capsule every eight hours) which he was to take for ten days and ten grams of ascorbic acid to be taken in half water and half citrus fruit juice each day for an indefinite period. He has remained well to-date.

TREATMENT

In the treatment of this particular syndrome two types of drugs are indicated. One drug to kill or neutralize the virus and/or toxins; the other type of drug to prevent or destroy secondary organisms. Ascorbic acid in adequate amounts is the drug of choice for the virus organism. Any one of the mold-derived drugs will adequately handle secondary invaders. In the case of ascorbic acid the amount employed will vary with the severity of the pathology, but in no instance should it be under 250 mg. per kg. of body weight. Clinical response will determine the time interval but it must be remembered that, like all other antibiotics, it *must* be given regularly around the clock. In such cases as we have described in this paper, the initial injections *must* be given by needle. In infants and small children the concentration should be 500 mg. per each one c.c. solution. Two to three grams can be given conveniently by the intramuscular route. Ice cubes held for several minutes to the gluteal muscles will practically eliminate the factor of pain. The intravenous route is always used in our practice in children four years or over. The concentration of ascorbic acid should be one gram per each five c.c. fluid when doses not exceeding 300 mg. per kg. of body weight are given. When doses from 300 mg. to 500 mg. are deemed necessary, and initially this is frequently the case, then the concentration should be 18 c.c. for each gram of the drug. Five per cent dextrose in water is the proper dilutant although there is no contraindication to the use of saline solution "per se." Following the initial injections and provided the patient can swallow and tolerate ascorbic acid orally, subsequent use of the drug should be by mouth. The contents of ampules can be added to citrus fruit juice, the crystals can be dissolved in plain tap water or one-half water and one-half juice; even the tablets can be crushed and added to juice or swallowed whole. Penicillin, triple sulfonamide and one of the tetracycline drugs is recommended for use with ascorbic acid. They can be used as a single unit or in any combination. Massive use of ascorbic acid is compatible with any other choice of drugs and in most instances it will enhance the value of these other remedies.

CONCLUSION

As we observed in June 1957, these cases are suggestive that the toxins of this particular virus or viruses act like a cephalic tetanus-toxemia and that it is not only possible but actually can culminate in diaphragmatic spasm, with dyspnoea and even asphyxia. We have referred to this as a "deadly syndrome" caused by an "insidious virus" and even though this is a fact proven, the condition is not new. The pathology is that previously recognized as "Acute Haemorrhagic Encephalitis." This form is always associated with infective diseases. It would seem that although any type of virus infection can progress to this final stage of encephalitis, that it would be most likely that one particular virus is responsible for this syndrome. In view of the fact that the majority of these cases have been seen during the epidemic season of "Red Measles" the causative agent would appear to be that of "morbilli." According to Wheeler and Jack's Handbook of Medicine, "this type of encephalitis attacks the grey and white, but especially the

grey matter of the mid and hind brain and of the cortex. The nuclei of cranial nerves are thus involved. The affected parts are found to be softened and show engorgement and thrombosis of vessels, haemorrhages, and proliferation of leucocytes, the nervous elements being destroyed." This haemorrhagic state is unmistakably a marked deficiency of ascorbic acid. The picture is clear. The history of a lingering cold or having had symptoms like the flu have *depleted* the body's supply of ascorbic acid beyond the daily normal requirements with an obvious break down of the capillary bed. This condition, in itself, demands the administration of large amount of ascorbic acid. Patients who have progressed to this stage, therefore, require massive doses of ascorbic acid and should they fail to receive this treatment, they will experience permanent nerve injury or lose their chance for survival. It is for this same reason, severe deficiency of ascorbic acid, that pregnant women are more susceptible to poliomyelitis than other women. Adequate ascorbic acid coverage can be followed by employing a two minute silver nitrate urine test or by checking the urine with qualitative Benedict's solution and ruling out the co-existence of sugar with the Tes-tape. The silver nitrate test³ is fast and accurate. Ten drops of 5% silver nitrate is placed into a Wasserman tube. To this is added 10 drops of a urine sample. Read in two minutes the test must show a color reaction of smoke gray to charcoal. If the Benedict's test is used the reaction will be from one to two plus for adequate ascorbic acid coverage, while at the same time the urine will show a negative Testape reaction. We feel that nasal oxygen is beneficial in these cases and should be used as supportive treatment. Maintaining proper Co₂ tension is probably equally as important. Here, too, ascorbic acid fits into the picture. Once ascorbic acid enters the blood a series of reactions are set up in which ascorbic acid drops at one phase molecules of water. The water molecule is then broken up, releasing wet oxygen and hydrogen. This wet oxygen tends to assist in the formation of Co₂. Critics will argue that cases such as we report here can be handled without the use of ascorbic acid. This is debatable. Many of these patients force citrus fruit juice to tolerance on their own, while others have only a partial recovery and still others die. With the use of massive doses of ascorbic acid I have yet to see a patient not fully recovered. Furthermore the use of large doses of ascorbic acid along with other antibiotics will shorten the illness by at least one-half the usual sickness days, and what is more important, they can be easily handled at home. The cases we report here were admitted for clinical evidence only, since many such cases have been treated successfully at their homes—even at the office with two and three visits a day for two days. Many such cases have been diagnosed, erroneously, as poliomyelitis. In fact it has often in the past been called "polioencephilitis." Wheeler and Jack's Handbook of Medicine⁴ lists under symptoms the following: "Sudden onset; headache, vomiting, convulsions, fever, drowsiness, leading to coma and death, or partial recovery." I would caution all physicians to remember that there is only one breath between life and death. This hesitancy on the part of physicians to use large amounts of ascorbic acid stems from the report that "all above 125 mg per day is spilled by way of the kidneys." This is a tragic error in judgment, and rests on the doorsteps of the National Research Council for attempting to allocate a set numerical unit for a chemical that can differ in each one of us either because of the individual kidney threshold level or because of greater

requirements necessitated by pathology. This point will be proven beyond question of doubt in a paper now being prepared covering 300 obstetrical patients. This brings to my mind a little ditty that I learned on my mother's knee, to wit: "How few think justly of the thinking few; how many never think who think they do."

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In this letter to the Editor of the *Tri-State Medical Journal*, Dr. Klenner states that ascorbic acid given intravenously is the "treatment of choice in carbon monoxide poisoning." He offers a biochemical model that might help explain ascorbic acid's effectiveness. He also suggests intravenous ascorbic acid is effective in treating barbiturate poisoning and puerperal sepsis caused by abortion.—*R.D.M.*

The Role of Ascorbic Acid in Therapeutics

Fred R. Klenner, M.D., Reidsville, N.C.

Tri-State Medical Journal, April 1959, Vol. 7, No. 2, p. 34

Ascorbic acid continues to play an important role in therapeutics. We have found ascorbic acid to be the treatment of choice in carbon monoxide poisoning, acute and chronic. A paper dealing with this, using dogs, will be sent for your consideration within the next several months. Since lives might be saved through this knowledge in the interim, a brief summary of the chemistry is in order. Hydrogen transport is of considerable importance in oxidative processes. Ascorbic acid serves well in this capacity. "Perfectly dry carbon monoxide and oxygen cannot unite to form carbon dioxide, but carbon monoxide and water may give rise to carbon dioxide in the complete absence of oxygen. The reactions which take place are: $\text{CO} + \text{H}_2\text{O} \rightarrow \text{HCOOH} \rightarrow \text{CO}_2 + \text{H}_2$ (Wright)." It is obvious that the oxygen of the water has been used to oxidize carbon monoxide to carbon dioxide with the liberation of hydrogen. It is true that hydrogen and oxygen remain tenaciously united, but if a *hydrogen acceptor* is available to take up the hydrogen, the oxygen becomes available for oxidative purposes. Glutathione, a tripeptide composed of cystine, glycine and glutamic acid, is available and "may facilitate cellular oxidation by acting as a hydrogen acceptor (Hopkins)," thus serving in the role of a catalyst to speed up the break-down of water.

Whenever ascorbic acid is given intravenously there is an immediate, spontaneous reaction in which it *drops* two molecules of water to form dehydroascorbic acid. Ascorbic acid further serves to make all cellular membranes more permeable. This *released* water is utilized in the reaction described above. The oxygen from this reaction not only joins up with the carbon monoxide, but also acts to increase the oxygen pressure. This increase in oxygen pressure is *assisted* by the accumulation of the 'newly and rapidly formed carbon dioxide,' which, in turn, tends to stimulate the respiratory center. This mass action displaces the carbon monoxide from its union with haemoglobin, restoring a normal state of the blood. The rapid formation of carbon dioxide and oxygen serves the same purpose as if the patient were given 7% carbon dioxide with 93% oxygen to breathe. The concentration of carbon dioxide never becomes pathological, since in the presence of a trace of alkali some of the carbon dioxide will combine to form carbonate, thus being displaced from solution. Blood *does* contain *alkali*, assuring this reaction. Some

of the released oxygen also becomes available for tissue utilization, counteracting the depressing action of CO-Hgb. on the dissociation curve of the functioning haemoglobin which is still present.

Another valuable use for ascorbic acid is in barbiturate poisoning. In our experience with a patient weighing 134 pounds, who had taken a lethal dose of a barbiturate, it apparently was the difference in the patient living. He was awake in 40 hours and fully recovered in 72 hours. 900 mg. of ascorbic acid per Kg. of body weight was given intravenously, in divided doses, the first 24 hours. 500 mg. per Kg. body weight was used in subsequent 24-hour periods, also given in divided doses. In this case ascorbic acid was used in conjunction with strychnine sulfate and metrazole given intra-muscularly and picrotoxin in isotonic saline given as a continuous drip (In this instance 64 mg. was given. All in the first 18 hours of treatment).

In another case, using 1200 mg. per Kg. of body weight the first 12 hours, in divided doses, and 600 mg. per Kg. body weight in subsequent 24-hour periods, in divided doses, a patient with advanced puerperal sepsis following a criminal abortion was *returned* to normal in 9 hours. Penicillin, sulfadiazine and I.V. Achromycin were also employed. The rapidity in which the pathology was reversed can hardly be attributed to these other antibiotics alone. This patient entered the hospital with 105.4° F. and in 9 hours it was 98.6° F. and remained so throughout the uneventful hospital stay.

Dr. Fred Klenner suggests that viral encephalitis can follow head and chest colds. Large doses of ascorbic acid administered by means of the needle can play a vital role in restoring the patient's health. Injected vitamin C, he says, not only destroys the responsible virus but also helps to maintain the integrity of the blood vessels in the brain. He speculates on routes viruses might take to enter the brain.—*R.D.M.*

Virus Encephalitis as a Sequela of the Pneumonias

Frederick R. Klenner, M.D., F.C.C.P., Reidsville, N.C.
Tri-State Medical Journal, February 1960, Vol. 7, No. 12, pp. 7–11

Every head cold must be considered as a probable source of brain pathology. Many cases of encephalitis precipitated by an attack of coryza will be of little significance and not recognized clinically. Some, however, will cripple; others will kill. This paper is presented in the hope that physicians will be on the alert for this insidious syndrome first described by Rosenfeld in 1903 under the caption "Brain Purpura or Haemorrhagic Encephalitis."

Many people have needlessly died through indifference on the part of the individual, a parent or guardian, even the physician. The so-called head cold is like a live ember in that it possesses the innate faculty of bursting into a consuming fire with the *next* breath of air pulled through the engorged nasal pathways. Frequently the "down-draft" is like a miniature tornado, transporting the microbes to the trachea as a tracheitis—a burning sensation in the region of the sternal notch. If not challenged with proper therapeutic agents, the main bronchus will be next. From the main bronchial tree the *flames of infection* extend out to the bronchioles as a bronchiolitis and then to the parenchyma of the lungs as a pneumonic reality. Often a pneumonitis exists without demonstrating too great incapacitation of the individual, who continues with his or her usual routine while attempting to alleviate the persisting head cold or nagging cough with a variety of combinations of home remedies. The physician has the responsibility to elicit this information from the patient, since such therapeutic measures will often cloud the true picture. Patients have died following the sudden development of cerebral manifestations, secondary to a slight head and/or chest cold because doctors were not impressed with their findings at the time of the initial examination or even with the history given by the individual, a relative, a friend. This is especially true in children, since children are not professional fakers to the extent that their behavior commands that they be carried for immediate medical consultation. It is better to *rule out* virus encephalitis by diligent observation and the employment of every laboratory procedure available that might lend assistance in the diagnosis rather than to have it *ruled in* at autopsy.

In an attempt to arrive at any definite etiological denominator, one must accept certain established clinical facts which tend to point to a common factor in all cases.

As pointed out by Baker and Noran,¹ in each type pneumonia cerebral complications of a *similar* clinical and pathological nature occur. This immediately speaks against the etiologic organism of the offending pneumonia as the probable agent causing the encephalitis. Baker and Noran suggested the possibility of a toxin responsible for this syndrome since scattered cerebral symptoms may occur in a toxemia secondary to pyrexia in any illness. They concede, however, that since severe cerebral manifestations are precipitated many times after the pneumonic process has subsided, or is only in the developing phase, that some other toxin, one not necessarily associated with the pyrexia but more directly related to the pneumonia and to the individual susceptibility to cerebral involvement. From a review of our own cases it can be stated categorically that in all near fatal illnesses the temperature was essentially normal; that is, one half degree either side of 98.6° F. initially. Ferraro² advanced the *allergic* theory, assuming that an allergic phenomenon took place in the central nervous system during the infectious disease. The consistency of the clinicopathologic picture found in these cases, in spite of the wide variety of pathologic organisms involved in the pneumonia, would tend to favor the *virus* concept.

Detection or awareness of this “brain” complication becomes of paramount importance, since severe cerebral residuals often follow relatively mild pulmonary inflammation. Comby, in 1907, was the first to call attention to this interesting *metastatic* sequela of the pneumonias. Although this nonpurulent type of encephalitis may follow every variety of pneumonia, the greater number will be associated with primary viral pneumonitis. This invasion of the lungs as the precursor of the encephalitis is always represented by mixed pathogens. When the pulmonary pathology is predominantly virus in origin, the secondary invaders will usually be found in the main bronchial tree and in the upper respiratory areas. When the pneumonic process is due to the staphylococcus or the pneumococcus the virus as the secondary invader can be present in all parts of the pulmonary system. When influenza is epidemic the pneumonia accompanying will be of the diffuse bronchial type yielding almost a pure culture of pneumococcus. This was the bacteriological and radiological findings during the recent flu epidemic in this area. All are aware of the possibilities of the staphylococcus, especially in infants, when chemotherapy has been pointed at every thing but gram positive organisms, or when “immunity” to *fashionable* drugs has been acquired by the micro-organisms because of the indiscriminate application of such drugs by the practicing physicians.

In a clinical problem such as these cases present, one must speculate on the pathway, as well as the manner, in which the virus gains entrance into the brain. The blood supply to this area definitely plays an important role. The arterial and venous channels as summarized by Wolff⁴ from the works of many investigators follow. The cerebral arterial tree, unlike that of many organs, has no hilus from which the vessels plunge into the body of the structure. Blood flowing to the brain through the internal carotid and vertebral arteries are united by the “Circle of Willis” which, with its six large branches, encircles the globoid hemispheres at their base. These trunks then divide into many smaller branches. A few enter the basal ganglia and choroid plexus, but for the most part they spread themselves like a net over the surface of the cortex. Smaller arteries at innumerable points dive deeply into the cortical and subcortical tissues where they

anastomose with one another and with others coming through the brain substance from the opposite surface of the hemisphere. The cerebral veins comprise two groups, the internal and external, with incomplete anastomoses between them. The internal group drains through the great vein of Galen, running back directly over the pineal body. The external veins emanate from the region of the insula. Because with growth there is anterior displacement of the frontal lobe, and posterior development of the main mass of the hemispheres, the direction of the terminal portion of the great veins is altered; the anterior veins are thus directed posteriorly and the posterior veins course obliquely anteriorly as they pass to the superior sagittal sinus. The large venous sinuses drain into channels at the base of the skull. The nerve control as given by Starling⁵ simply states that the brain, as the master tissue of the body, and acting through the medullary centers, controls the circulation through all other parts of the body. In maintaining normal function the brain requires a certain blood supply which is dependent on the pressure in the carotid arteries and Circle of Willis. If this pressure fails, the function of the brain will be affected and loss of consciousness rapidly ensues. The alarming increased respiratory rate seen in many of the "encephalitic" patients strongly suggests that cerebral compression and/or abnormal *vagal* stimulation is taking place. The depth of the pulmonary pull will also be exaggerated and might be used as an index in determining the type and degree of involvement of the central nervous system. Hyperpnea in such instances is involuntary. It is probable that due to an increase in hydrogen ions in the respiratory center itself,⁶ secondary to impaired blood flow through the inflamed lungs, may be the activating factor. This forced and sometimes labored breathing, but not Kussamaul in type, results from insufficient oxygen supply to the respiratory center and in some part to acid production within the center itself. Under abnormal conditions,⁷ including various diseased conditions, the possibility of a "frank" acidosis being a potential cause of oedema is quite plausible. This syndrome alone would account for the clinical manifestations of headache, irritability, anorexia, abdominal cramps, weakness, coma and sometimes *death*.

Baker and Noran enumerate five groups, each showing certain definite clinical characteristics which may be of both diagnostic and prognostic significance in relation to this *virus* syndrome: (1) Symptoms of a nonspecific nature (headache, vomiting, irritability); (2) delirious type; (3) convulsive type; (4) lethargic type; (5) hemiplegic type. These groups plus two additional types, namely, (6) blood invasion type and (7) allergic rhinitis type were reported by me in the *Tri-State Medical Journal*, October 1958. This report was made on the basis of actual cases treated in our local hospital without knowledge of the Baker-Noran publication. This factor is emphasized to show the frequency in which this pathology presents itself and to call attention to the "stereo-types" which should make the clinical recognition elementary. Occasionally one will find overlapping of the groups. One case, in an adult, began with convulsive seizures which finally demonstrated paralysis. Irritability and increasing severity of headache over a period of several days was the history given by both our cases showing the delirious type. In spite of this obvious picture, many patients die with the diagnosis *labeled* pneumonia, nephritis, rheumatic fever, cerebral haemorrhage—anything but *virus encephalitis*.

It is possible for the virus to gain entrance into the cerebral structures by several routes: (1) Through the olfactory nerves; (2) direct extension from otitis media; (3) through the portals of the stomach from material swallowed from pulmonary and/or upper respiratory drainage; (4) the blood stream. After arriving in the brain the virus goes through the blood cerebro spinal fluid barrier and/or the blood brain barrier by one of three ways: (1) Electrical charge; (2) chemical lysis of tissue; (3) osmosis. Wittgestine and Krebs, 1926, reported that the *choroid plexus* is impermeable to basic dye while the *capillary system* of the brain, although permeable to acid dye, is much more susceptible for the passage of basic dye. Friedeman and Elkeles in 1930 and Schmid in 1931 demonstrated the existence of a reverse relationship between the blood brain barrier (B.B.B.) and the blood cerebro spinal fluid barrier (B.C.S.F.B.) in that by dye experiments it was shown that the B.B.B. is more permeable for basic dye while the B.C.S.F.B. is more permeable for acid dye. Bakay⁸ reported that the permeability of the B.B.B. can be changed by introducing various toxic agents into the blood circulation. The effect of these agents is only temporary and the "barrier" usually regains its normal function within minutes or hours following their application unless the plasma concentration of the toxins is kept at a constant high level. Spatz (1933) found that the penetration into the brain of acid dyes depended on their particle size. Diffusion rather than hydro-dynamic flow constitutes the chief process whereby small molecules can exchange rapidly between plasma and interstitial fluid. Other investigators report that the permeability of the cerebral capillaries rests with its electrical charge. The B.B.B. protects the central nervous system from negatively charged toxins. On the other hand the cerebral capillaries are permeable to substances carrying a positive or no charge at the pH of the blood, while they are impermeable to those carrying negative charge. In recent investigations Chambers and Zweifach¹⁰ emphasized the importance of the intercellular cement of the capillary wall in regulating permeability of the blood vessels of the central nervous system. Many scientists believe that the "barrier" *resides* in the intima of the cerebral vessels and that it possesses selective action in the transfer of certain ions from the blood into the brain.

Case History No. 1: 58-year-old white female seen at her home 24 hours prior to hospital admission. History of slight head and chest cold for period of 10 days. Examination revealed nothing remarkable. Appropriate therapeutic measures taken. Reported much improved 12 hours later. Admitted to local hospital 24 hours following initial visit because of convulsive seizure. Patient experienced three additional convulsions. Admission temp. 100.8° F., pulse 140, Resp. 32. Extremely restless. Was given 24 grams ascorbic acid with 350 c.c. 5D in water I.V. for three times at 8 hours intervals. Digifortis Amp. 1 for 7 times then q 2 h until digitalized. Metrazol 0.1 gm given I.M. q 8 h. Ilosone 250 mg q 4 h as supportive treatment. Four grams ascorbic acid given in orange juice q 4 h. Twenty-four hours following admission patient was awake and rational but completely paralyzed right arm and leg. This cleared completely after 48 hours. Oxygen, nasal, given 5 liters per minute. Lyo-B-C was given with 6 grams ascorbic acid I.V. daily for 8 days. The patient was well of her virus infection by the fourth hospital day. She was however a severe cardiac and because of a diet psychosis for years required weeks of

hospital stay to return her to her usual routine. Classical pellagra was also treated and corrected during this hospital admission.

Case History No. 2: 23-year-old white male. Seen in emergency room local hospital in semicoma. Friends stated that he was found unconscious in telephone booth. Temp. 98.6° F., pulse 130, respirations 34 per minute, extremely labored. Pupils dilated. Subsequently patient narrated that he had had a cold for two weeks. Experienced headache for period of five days prior to hospital admission. He had consulted another physician the day of admission because he could no longer endure the severe headache which failed to respond to excessive doses of usual remedies. He was given 30 grams of ascorbic acid in 350 5D water I.V. Approximately 30 minutes following admission and shortly after fluids were started he became violently disorientated requiring four men to hold him on the bed. This continued for about five hours after which his recovery was uneventful. The initial order for ascorbic acid was repeated at 8 hour intervals for five times. Following the intravenous medication, ascorbic acid was given 4 to 6 grams in juice every 4 to 6 hours. His WBC was 7000 with a normal differential. He was sent to a teaching hospital by request of his parents after 6 hospital days where the impression of viral encephalitis was confirmed. He received no treatment at this second institution and was discharged to his home following completion of his examination. Achromycin V 250 mg. was given every 4 hours for 12 times.

Case History No. 3: 22-year-old male first seen in emergency room of local hospital where he was reported to be in an unconscious state. Upon arrival at the hospital, however, I found the patient on the floor, being held down by seven men while an attempt was made to bind his legs and arms with sheets. This did not hold patient and within minutes he was loose, up on his feet and swinging wildly at anything that came in his way. He was subdued by grasping one arm at the wrist and the other hand of the subduer was "attached" to the patient's hair which was pulled with force in a backward direction. With this hold the patient allowed himself to be placed on a stretcher and arms and legs tied to each corner with sheets. After recovery the patient did not remember this episode. He remained rather agitated for about four hours after which time he was a model. We elicited the history on the second day that he had been irritable for the entire week before this incident; he could not get along with anyone. On the day of hospital admission he saw a second physician because he believed his severe abdominal pain might be associated with a recent haemorrhoid operation. He had had a dull to severe headache for several days but attributed this to a sinus condition, although he remembered telling a relative that the pain was different than what he usually experienced. He did not have the prescriptions filled that were given to him by the surgeon. Later the same day he accompanied a friend on a short trip during which time he suddenly developed extreme head pains, severe nausea and profound weakness. He telephoned a relative to come get him and take him home. He collapsed as he left the telephone booth and was believed dead. The ambulance driver confided that he too believed the boy dead and brought him to the hospital for confirmation. Temp. was 98.4° F., pulse 146, respirations 28 per minute. He was given 50 mg. thorazine by needle

in an effort to control his restlessness. Ascorbic acid was given in massive doses, 100 grams intravenously the first 24 hours. Subsequent doses consisted of 4 grams in juice q 4 to 6 hours. Penicillin was employed for secondary invaders. He experienced severe nose bleed on the 6th hospital day requiring a classical pack. Calcium gluconate 10 c.c. was given I.V. for two times with the thinking that high doses of ascorbic might have removed calcium ions in excess by way of oxalic acid as the calcium salt.

SUMMARY

Virus encephalitis as a sequela of the pneumonias is more common than the literature would suggest. This error exists because physicians no longer take or have the time to read and reflect. This error exists because physicians are inclined to make their diagnosis from laboratory reports rather than with the use of the stethoscope and their brain. There are many pathological conditions in which similarity tends to mislead. If this paper provokes those physicians who read it to consider the possibility of cerebral complications with lingering head and/or chest colds, our efforts will have been rewarded. We must not gamble with the simple head cold.

I cannot but wonder if in the picture portrayed here there lies the factor of "genetical error." Certainly in both cases described as presenting delirious manifestations there is sufficient evidence to warrant such a hypothesis. All the factors presented as an explanation could still follow, their realization being precipitated due to fault in genetics.

The cases that we have seen and successfully treated definitely follow a set pattern so stereotype that once looked for will never be forgotten. Two of our cases demonstrated hemiplegia; five cases had convulsive seizures; four cases abruptly started with stupor or were of the lethargic type; three cases started with a severe shaking chill. Strangling during the course of normal eating and definitely due to nerve paralysis, one case. Many other cases represented the non-specific type and I am sure many, many more cases of a minor nature went undetected.

There is much information available which indicates that the oxidation rate and vascularity may be related. Oxygen consumption of the brain is large, ranking the cerebrum among the more actively metabolizing organs of the body. Interference with the blood supply of the central nervous system can be quickly disastrous, since the brain cannot accumulate an oxygen debt.

The possible routes of invasion by the virus have been outlined along with the manner in which the virus gains entrance into the brain substance.

The importance of the intercellular cement of the capillary wall in regulating permeability of the blood vessels of the central nervous system would suggest also the *importance* of administering large doses of ascorbic acid in order to maintain the integrity of these structures. Especially must this be true if the "barrier" to the brain is associated with the intima of the blood vessels. Large doses of ascorbic acid are necessary also as a chemical to destroy the virus organism. Recently I treated a seven-year-old child, off and on over a period of six weeks, for influenza like symptoms. Therapy included one of the mold derived drugs, sulfadiazine, and moderate doses of ascorbic acid. On three different episodes this type of therapy was dramatically effective. When the child became ill for the fourth time, the administration of the above antibiotics had no reversing action. On

the third day the child suddenly became lethargic, began to run as much as 102.6° F. At this point all medication was discontinued except that I began to give six grams ascorbic acid intravenously every 6 hours. During the same time 10 grams ascorbic acid were given by mouth. The recovery was spontaneous in 24 hours. I had ample opportunity to observe this case—the child was my son.

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Symptomectomy

A chat with Robert Cathcart, M.D.

B. J. Luberoff

Incline Village, Nevada, is a community of 5000 souls, more or less, except during skiing season. Then it swells beyond 15 000. It's on the North shore of Lake Tahoe, a beautiful hour's drive over Mt. Rose from Reno.

Make believe that you're there, sitting in the living room of the 5000 square foot lakeshore home designed by Robert Fulton Cathcart, III, M.D. There's a fire crackling in his wall to wall, floor to ceiling stone fireplace. The first thing you might want to ask him is how in the world he came to practice medicine in Incline Village? Did it have anything to do with his being an orthopedic surgeon and how some people ski?

Well I had the chance to spend such an evening with Bob Cathcart and to ask him that question, and some others. Here's how it went.



Incline Village, Nev.; Mt. Rose is in the background

Caution

This article is only for a mature audience. The views expressed here are unorthodox and do not necessarily represent those of the American Chemical Society; while Dr. Cathcart says, "What I've told you represents my experience up to today. It could all change tomorrow. No guarantees expressed or implied." He further stressed that he does not advocate giving any medication without the intervention of a physician.

A. Orthopedics isn't what really brought me here. I had practiced five years in San Mateo—that's on the San Francisco peninsula. During that period I invented and patented what's now a widely-used hip prosthesis . . . we can talk about it later . . . but then I became interested in nutrition, specifically vitamin C. After reading Pauling and everything else I could on the subject, I started "experimenting" with vitamin C first on myself and the family and then on a few selected patients. I made some basic discoveries, and it's them I really want to tell you about.

Now in San Mateo I had little opportunity to treat patients with vitamin C. Peer pressure at that time, about seven years ago, was pretty much against the physician using vitamin C. Besides, as an orthopedic surgeon, in a region where specialization was respected, I seldom saw patients who had colds, or other viral diseases. So I commuted to Incline Village every week for a year. It's only a few hours from San Francisco. Here I went into association with a general practitioner who planned to go to another town after about a year. During that year I demonstrated that *properly used*, vitamin C could decrease most of the morbidity and all of the mortality from viral diseases. I contacted Pauling about this and he said that he knew of no other physician who was doing exactly what I was doing.

Q. What was that?

A. Well first let me give you some background. Fred Klenner of Reidsville (1), North Carolina, one of the greats in vitamin C therapy, has been working with it for what seems like twenty or thirty years. He found that he could detoxify most virus diseases with intravenous doses of "C". Now he even uses it for carbon monoxide poisoning, barbiturate poisoning, even snake bites. Now what I discovered, which was different, is this: the average person, at least 80% of normal individuals, when they are well can take, orally, between 10 and 15 grams of vitamin C, in divided doses, during the day before—

Q. Hold on, did you say 10 to 15 *grams*?

A. That's correct, 10 to 15 *thousand* milligrams a day. Most people can take that much before it produces diarrhea. Some people can tolerate less, a few can take more . . . *when they're well*. The astonishing thing is that this same person . . . the patient who when well gets diarrhea on say 12 grams . . . when ill with a moderate cold can take 30 to 60 grams without diarrhea; with a bad cold or a flu, 100 grams, sometimes even 150 grams, and with viral diseases such as mononucleosis or viral pneumonias, I've used in excess of 200 grams a day without it producing diarrhea . . .

Q. That's nearly a half pound . . .

A. That's correct. In some cases the body evidently

with vitamin C

needs that much, albeit for only a short time. With mononucleosis or viral pneumonias, during the first couple days of the disease we sometimes see a need for that half pound—more or less. Patients with bacterial diseases will absorb similar amounts depending on level of toxicity. Of course, they should get the appropriate antibiotic, too. Essentially, the sicker you are the more you can take; and taking enough—and *that's important*—seems to detoxify you. You get well quickly. And as you do you find that you can tolerate less and less ascorbic acid until you go back to normal when you're well.

Now there's been a lot of talk about double blind studies and about the benefits of vitamin C in preventing colds and things like that. Your article by Coulehan (2) is a case in point . . .

Q. Let me slow you down just a minute. What you're saying is that an average, healthy person can take about 10 grams a day. If he's well and takes much more he'll begin to feel malaise in the gastrointestinal system, and if he persists he'll get diarrhea.

A. Right.

Q. But if he has a viral illness then he can take a lot more, and doing so will make him feel very much better, very fast. What's this saying about what is happening in the GI system and elsewhere?

A. Well, we think that ingested vitamin C in the GI system is in equilibrium, you might say, with that in the bloodstream. It's absorbed through the stomach and the intestines into the blood stream to maintain some kind of "saturation" there. Now if, for whatever purpose, the blood is "throwing off" the vitamin C at a high rate, then more and more will be absorbed so that the vitamin C in the intestine does not reach the rectum. If it does in sufficient amount to create a hypertonic situation, then body fluids migrate to dilute it and that produces mild diarrhea.

Our genetic defect

Q. So you kind of "titrate" the illness. But if the body really needed all that ascorbic acid, wouldn't it just make it?

A. Ah, that's the point—it *can't*. Irwin Stone (3) and others say that man has some sort of genetic defect, that in the evolutionary process the higher primates lost the ability to synthesize ascorbic acid. Only a few other animals share this "defect": the guinea pig and an African fruit-eating bat and some minor species. By and large the lower animals synthesize ascorbic acid in the kidneys; higher up the evolutionary tree, they make it in the liver. It really is a liver metabolite in higher animals. Now how did this happen? Well, the higher primates evolved in areas that had fruits and vegetables in profusion. Just think of the monkey sitting around eating bananas and



leafy things that have a lot of ascorbic acid. He was fit enough to survive in this environment. The stresses on him were not great. He was not exposed to as many infectious diseases as we are. So the ability to synthesize vitamin C offered little survival value and was lost. Now along came man with his great capability and curiosity, and he ventured out from these Gardens of Eden and went into areas where food ascorbic acid was scarce. His diet changed. The biggest change came when he went out on the sea. There, without any fruits and vegetables, he got scurvy, that's the acute deprivation of vitamin C. It was only when the British discovered that lime juice could prevent scurvy (8) that men were able to go for long distances out on the sea. Scurvy will be induced in two to three months if you're on a completely vitamin C free diet. Then you'll start manifesting symptoms of the disease and without treatment you'll die in another month or so. But preceding the scurvy syndrome are a variety of low blood ascorbic acid states. Stone and Pauling popularized them and pointed out that they lead to various diseases from which mankind suffers.

Q. What does ascorbic acid do normally?

A. The non-controversial functions of ascorbic acid (4-6) include several enzymatic processes, the body's ability to make collagen, dentine, adrenalin, corticoste-

a person dies after an illness, the body contains almost no ascorbic acid.

Now isn't it striking how many people who have been admitted to the hospital with one disease get phlebitis, or a heart attack, or a stroke, all disorders of the vitamin C sensitive blood clotting system? Or they get pneumonia, a disorder of the immune system. How many illnesses seem to occur after a period of physical stress, after some previous disease, viral, bacterial? There's even been work that relates emotional stress to physical disease. Well, it just figures that if we see some chemical run down under stress we ought to try to replace it.

Q. Fair enough—but how much do you need? How much, for instance, do other animals make? Well ones.

A. The goat is often taken as a reference point because he weighs about the same as a person.

Q. And because he, too, eats a capricious diet?

A. Well . . . no . . . anyway a 70-kilogram goat will make about 13 grams of vitamin C a day.

Q. In light of that, the numbers you mention, 10 to 15 grams for a healthy adult human, is not totally inconceivable. How about other models?

A. Several other animals have been assayed. These are ballpark figures for most of them. Cats and dogs make ascorbic acid, but perhaps they can't always make as much as might be ideal so they suffer from such toxic diseases as distemper. A veterinarian in San Jose has been curing distemper with ascorbic acid injections (9).

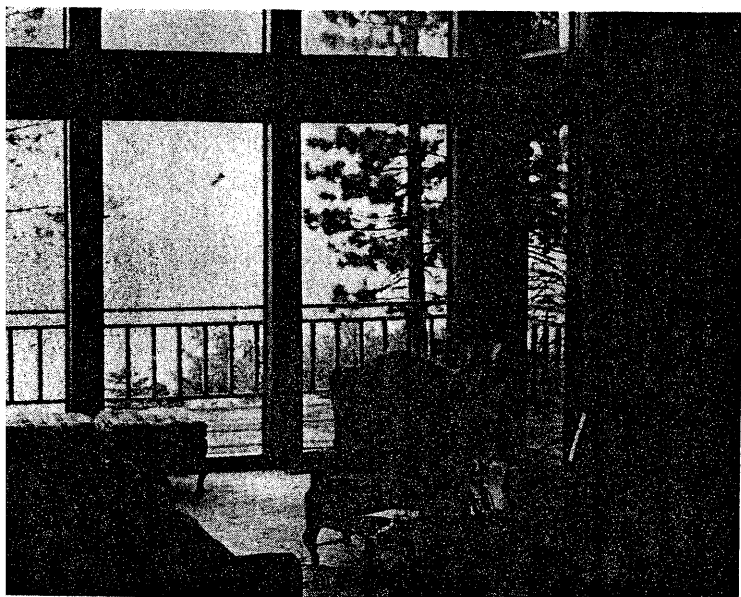
Isn't it interesting, when you reflect on it, that the guinea pig, who can't make vitamin C, is a generally accepted model for testing human diseases? I've often said, tongue-in-cheek of course, that if you've got a disease you can't give to anything but man, monkey, and guinea pig, you've got a sure bet that you can cure it with vitamin C.

Clinical insight

Q. OK, let's go back to curing things. You referred me to Lewin's new book (7). It's very thorough and goes to great length in its discussions of modes and mechanisms of action and metabolic pathways and so forth. As a biochemist that's about all Lewin can do. Now we may not understand how the body is doing whatever it's doing, but people will get sick and have to be treated. You approached things pragmatically. You treat patients. Tell us about that.

A. My practice is to let the body take as much vitamin C as it needs . . . take an amount proportional to the amount of toxin that's around. Remember, everyone else has been talking about a *fixed* dose, usually at what I consider to be only a homeopathic level. Their studies go from 2 to maybe 4 grams a day and they see little clinical effect and none statistically. That doesn't surprise me. Such doses simply do not take on a disease after it's established. So that if you have a 100-gram cold . . . it's my custom to put a number before the name of a disease to represent the amount of vitamin C which that patient can consume the first couple of days of the disease without diarrhea . . . so that if you have a 100-gram cold and the patient is taking roughly 100 grams a day, you will quickly eliminate perhaps 90% of the symptoms of the disease. But if you treat that same cold with 2 grams or even 20 grams a day you won't see much happen. In some cases, especially if treated early, it almost seems as if megadoses were killing viruses.

With bad colds or influenza we don't seem to shorten



roids, maintain proper functioning of the immune system, the blood coagulation system, metabolism of several amino acids. Lewin (7) believes that ascorbate aids in formation of cyclic AMP and inhibits its hydrolysis which, if true, means that vitamin C indirectly affects almost every hormone function . . .

Q. That's quite a spectrum of different kinds of activity.

A. That's right, and everyone agrees on the need of ascorbic acid here. The quarrel is over how much is needed for these functions. When someone is well, the amount needed may be small. But what happens when he's ill? What attracted me is that if someone dies suddenly; say has been killed instantly in an automobile accident, then his tissues contain a lot of ascorbic acid. (The adrenal glands have the highest concentration.) However, when

the duration of the infection, but we render patients sufficiently asymptomatic so that they weather the infection without complications. Most of the time my patients don't have to miss any work time. If you're using enough ascorbic acid it will promptly take a fever down to normal, and you won't have the normal aches and pains of flu-like diseases.

Q. So we're talking about treatment versus prevention. That seems a little hard to demonstrate in a normal double blind experiment: the dose has to be tailored to the individual's disease and to its stage. Before we look further at that problem—and it's a real one—let me ask you to share more of your clinical experiences.

Pneumonia

A. Let me give you a typical case, a lady here, about, oh, 28, developed viral pneumonia. As far as I could tell she did not respond to antibiotics and she never did "culture" any place. When she presented herself she was very ill, high temperature, the right upper lobe infiltrated with the pneumonia process; difficulty breathing. So we hooked her up to intravenous ascorbic acid, about 1 gram per 18 cc's, and ran it in just as fast as we could. I gave her about 55 grams by vein and the remainder orally, about 215 grams went into her between 11 o'clock in the morning and 9 o'clock that night, at which time the pneumonia went into crisis. She drenched three sets of bed clothing that night. The next morning she was feeling much better. We did the same thing the next day. She returned to work less than a week after I first saw her. We have daily x-rays that demonstrate the rapid dissolution of the pneumonia process.

At that time I treated two other people in town who had the same thing, and got similar results. Three other patients in town went to other physicians and were hospitalized about two weeks and weren't much better when they came out.

Q. I'm sure a lot of scientists will say "Well that's just anecdotal . . ." To me it seems that when we don't know how a therapy works or can't demonstrate efficacy in a rigid protocol, then we have to rely on individual clinical experience.

You'll recall that I first contacted you because I suspected that vitamin C might have some value in treating my son's mononucleosis, a very debilitating disease particularly common among students. It knocked my son out for the entire summer and we were told that it has no treatment, other than lots of rest. Can you do anything with mono?

Mono

A. The first patient that I ran into with it was a junior high school librarian who was about 22 and weighed about 100 pounds wringing wet. She came in with a severe case of mononucleosis. I told her about the bowel tolerance idea and explained to her how to do this self-titration. I saw her three or four days later; she was almost completely well.

Q. This lady really had mono?

A. Oh yes. Mononucleosis is a disease we can spot without a tremendous amount of lab work. Usually you do a heterophile test and look at the white cells. A positive is quite definitive; a negative can be misleading.

The typical patient who gets mononucleosis is exactly

the one who does the best on vitamin C: older teenagers or young adults are just fantastic vitamin C takers. They can understand the bowel tolerance idea, have iron stomachs, and couldn't care less about slight gas and diarrhea when they have this horrible disease . . . In fact the sicker a patient is the better he does because the relief of symptoms is so dramatic that they don't need any arguments to convince them to continue treatment. So what usually happens is that in three to five days the symptoms are 90% relieved. Then some get the message loud and clear: if they stop the vitamin C too soon they get sick all over again.

The infection may go on just about as long as it would have in the first place, but the person is functional and doesn't develop complications. He can go back to school or work or whatever. But he must continue to take vitamin C doses as high as the bowel will tolerate. It can be many months, sometimes a year, before he's down to a normal 10-15 grams per day. He just titrates between relief of most symptoms and diarrhea. The titer will decrease from day to day unless he stops taking the vitamin C. Then there's a resurgence of the disease, and you go up to higher doses again and bring it back down.

The important thing with mono or other responsive dis-



eases is that we can get people back to work in days. You know we're in ski country here. I would be unhappy if one of my ski patrols wasn't back on duty within a week or ten days after having contracted mononucleosis.

Q. This is a disease that has a unique, positive diagnosis, so it's not possible that we're seeing some kind of artifact. You're sure that you're seeing mono?

Hepatitis

A. Oh, sure. The other disease that is very specific is infectious hepatitis. Let me tell you about it. It's a cinch for vitamin C. The difference between the course of the disease with and without vitamin C is quite obvious if only because hepatitis is a disease that we can put numbers on. There are various enzyme systems that we can follow to

Let me explain . . .

"If the doctor gives too little information, he or she may be sued for having failed to inform a patient of the risks. But if the doctor describes the risks too persuasively, the patient may be frightened away from a needed procedure. In a recent case a widow sued a doctor for frightening her late husband away from an operation that might have saved his life."

Consumer Reports, Sept. 1977

Lawbook medicine

"Few physicians stopped practicing, but some claimed that the possibility of a malpractice suit forced them into "defensive medicine"—forgoing what they judged to be the best treatment or choosing unnecessarily complicated and expensive diagnostic studies in order to limit legal liability.

"Finally, it was claimed that the cost of malpractice insurance would deter young physicians from entering such high-risk specialties as orthopedics, neurosurgery, anesthesiology, and obstetrics."

Consumer Reports, Sept. 1977

Not bad

"For all obstetricians in office practice, the median net compensation after practice expenses (including insurance) came to \$72,380. It would seem that the economic incentive to enter that particular specialty has not disappeared."

Consumer Reports, Sept. 1977

Too small

"Few lawyers care to take on "small" cases—those where the damages are a few hundred or a few thousand dollars. "In our office, we use \$100,000 as a cutoff," says Robert Begam, past-president of the Association of Trial Lawyers of America. "The economics of handling medical malpractice cases are such that unless a lengthy period of disability is involved we won't handle it. We expect to put in 500 to 1000 hours on a case, and to incur \$10,000 to \$25,000 in expenses, before we find out whether we'll get any return."

Consumer Reports, Nov. 1977

Channeling

"Channeling" consists of making hospitals legally responsible for all acts of medical malpractice that occur within their walls. Doctors and other individual providers would be relieved of legal responsibility, though they might still bear some financial responsibility.

"Channeling, it is argued, would give hospitals the incentive to exercise closer supervision over their medical staffs. Most hospitals are staffed by physicians in private practice, who, in effect, use the hospital as a workshop. Supervision is exercised to a degree through various committees of the medical staff, including credentials committees, tissue committees, and others. However, while the committees almost always exist on paper, as a condition for a hospital's accreditation, their effectiveness varies greatly among hospitals. If held legally responsible for all medical errors made inside their walls, hospitals would have to make sure the medical staff polices itself effectively. Hospitals would also have to gain a more precise idea of which procedures entail the most risk and which individuals are making the most errors. More careful review of applicants for staff privileges (use of the hospital) and better pruning of medical staffs might result.

"The idea of channeling for medical malpractice was originally put forward by John G. Day, The Insurance Commissioner of Virginia. He estimated that about 80 percent of all medical malpractice suits arose out of incidents in hospital settings. New data compiled by the National Association of Insurance Commissioners show that Day's figure was almost exactly correct.

Consumer Reports, Nov. 1977

show the course of the disease. Infectious hepatitis can be mild where the patient is just a little yellow and maybe a bit tender in the abdomen, but not very sick. But the patients I'm talking about—20 of them, at least—were profoundly ill with hepatitis, and here again we were able to detoxify them in three to five days. The patient is feeling essentially well in three to four days. It generally takes about six days for the jaundice to clear. In two to three days the urine returns to normal color. (You see, with hepatitis the bile is blocked in the liver so that the urine turns brown and the stool turns clay white.)

Hepatitis is a serious problem following blood transfusions. As a matter of fact the whole system of gathering blood in this country is undergoing revision because people who sell their blood have a high incidence of hepatitis. That's why they're trying to go completely to a voluntary system. I'm not sure that's necessary because it's apparently so simple to control hepatitis: just give patients vitamin C after blood transfusions. One Japanese physician (10) has shown that his patients don't get hepatitis if he puts them on maintenance doses of ascorbic acid following blood transfusions. Anybody who is stressed enough to need a blood transfusion should be getting large doses of vitamin C anyway.

Psychoactivity

Q. You use the term stress. To the layman that means psychological stress. Do you mean to imply that vitamin C has any benefit in that kind of situation?

A. I've been using the term stress in its broadest medical sense, but the average person under mental stress can often take a few grams more than he could ordinarily tolerate. Patients who do, say that they feel better and subjectively think that they can meet the stress better.

Vitamin C is definitely psychoactive (11). Schizophrenic patients require 10 times as much vitamin C as others to develop the same ascorbic acid level in their urine.

A Dr. Libby (12) in Los Angeles discovered that ascorbic acid or sodium ascorbate, I think he uses about 60 grams a day, can detoxify heroin addicts almost immediately. (He administers a protein extract with the "C" because he found heroin addicts to be low in proteins.) I had a little experience in this but didn't have enough patients here to follow up on it. Libby practices near a Methadone Center. He found that on his program, patients get no effect from the fix. If they take their 60 grams of sodium ascorbate they can do the heroin and it has no effect whatsoever; later they find they have no withdrawal symptoms, and soon give it up. Heroin addicts mostly want to give up their addiction, but previously all they had was a choice between feeling rotten and feeling horrible.

You know, Stone feels that there is a receptor site in the brain that would be filled by ascorbic acid if there were enough (12). But instead that site is filled with such things as heroin or morphine or barbituates. One end of the molecule fits in where ascorbic acid ought to fit but the other end sticks out and that's what does the crazy thing. Well, if you give ascorbic acid, it displaces the unwanted molecule and also blocks the need for it, so no withdrawal symptoms.

Side effects

Physicians have difficulty in thinking of something that does so many different things. We're used to medicines

that are fairly specific. Now ascorbic acid has these myriad, noncontroversial functions that go on in many many different systems of the body. Essentially what I found is that by giving huge amounts of ascorbic acid, it would tune up, if you will, all of these functions to high efficiency, far more than what's been experienced with the lower doses. Some of the enemies of ascorbic acid point out that there is no ascorbic acid in the body when a person is sick, yet he gets well anyway. They say that proves that you don't need ascorbic acid. It's like recommending that a football coach hold his first team on the bench because he's just barely winning with his second team.

Q. OK. So with all that we must come around to why this megadose therapy isn't widely used. The first thing that comes to mind is that it must have some absolutely terrible side effects. What would you say is the worst side effect other than diarrhea that ascorbic acid produces?

A. Well some people don't like the taste.

Q. And that you call a terrible side effect?

A. Certain patients feel they have trouble with acids in general. They are usually nonspecific about it and have avoided oranges, lemons, grapefruit, and things like that all their lives. These people frequently have a lot of difficulties late in life, I think because they're unusually low in vitamin C. Some patients do indeed have difficulties in first taking ascorbic acid.

Q. How about sodium ascorbate?

A. I've been reluctant to use large amounts of sodium ascorbate—that's a friendly differences between Stone and me. Stone feels that the problems people get into when they take large amounts of sodium could be avoided by taking sodium ascorbate. For instance the hypertensive, who shouldn't eat large amounts of sodium, wouldn't have been hypertensive in the first place if he or she had taken large amounts of ascorbic acid all his life. Well that may be true, but when I see a patient with an acute viral disease I don't want to flood his system with sodium. Imagine how much sodium is needed to neutralize 200 grams of ascorbic acid. So I use the free acid. One in a couple thousand may break out in a rash about the face or soft parts. This is transient and, usually, if they persist in their vitamin C régime, it goes away.

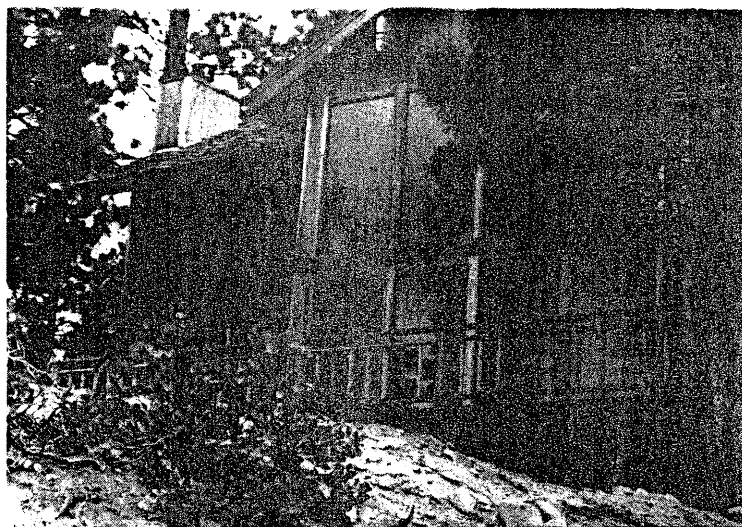
Many people who are intolerant to vitamin C by mouth become tolerant after a few days on intravenous vitamin C. I've never found a person who was intolerant to vitamin C injections.

People who have ulcers sometimes don't tolerate ascorbic acid. Interestingly half the people with ulcers swear that they get well with vitamin C and the other half say they get worse. I'm not entirely sure why that is.

Q. How about kidney stones?

A. I've never seen an oxalate kidney stone among my regular vitamin C takers. There is a theory that says that ascorbic acid breaks down to oxalate so that if a person had difficulty handling oxalate he could precipitate oxalate stones. But the situation is paradoxical: I'll grant that if a person did have difficulty handling oxalates, and he took maybe 500 mg of ascorbic acid a day, he might increase his oxalate load, but the paradox is that if a person takes the powder in large doses, as large as I've been talking about, it somehow makes the oxalate more soluble in the urine. (Ed: Cation chelation?) Anyway, the pragmatic fact is that in my experience oxalate stones caused by vitamin C are not something to worry about.

I have had four patients complain that they had some



Cathcart on malpractice

Now that I have a house and a family and so many responsibilities I wouldn't dream of trying to apply this technology in view of the present malpractice crisis.

If the Federal Government would lay off and consumer advocates understand health care delivery, then market pressures would rapidly bring into being things people need. All the do-gooders, the people who would like to protect us from malpractice, are doing the exact opposite of what they set out to do and they're doing it in a big way. Technological advance renders malpractice and incompetence almost insignificant. Today the least competent doctor can prevent polio better than the best physician could treat it 30 years ago. Studies on ascorbic acid that I was starting with post-operative patients just as I quit surgery were yielding results which, if pursued, probably would have alone decreased the annual morbidity from surgery far more than all of the morbidity involved in malpractice suits in a year in the United States. But we're afraid of new things and as long as we are we're not going to get them. This fear retardation accumulates like compound interest. Research accumulates like compound interest; it builds on itself. If something new is delayed we're stuck with that delay forever. The amount of human suffering for the remainder of history of mankind caused by unreasonable fear retardation, by this loss of compounding of interest in clinical research, means that we are causing astronomical amounts of human suffering.

burning sensation on urinating when they took large doses of ascorbic acid, but I've certainly never seen anything like the report that came out shortly after Pauling's book that in Europe, where they use ascorbic acid in the treatment of tuberculosis, that screaming could be heard from the sanatorium men's room. My experience with this is vast and I can say without qualification that that story is an absolute lie. It does not happen. The other thing that has been said is based on a study by Victor Herbert (13) that indicated that vitamin C blocked vitamin B-12 metabolism. This was front page news; but I understand that other studies indicate that there were some difficulties with his tests *in vitro* and that, indeed, this does not happen in humans. In any event, I have never seen any evidence of B-12 blockage or pernicious anemia. As a matter

of fact our patients seem to have pretty thick blood. Of course we're here at high altitude so we could expect that.

In summary then, I find no difficulty whatsoever, except those minor things I've mentioned.

Q. No side effects. Doctor, to how many patients would you estimate you've given megadoses of vitamin C?

A. I think it's been about 7000 patients over the last 10 years. During epidemics in my village, the local pharmacies have sold as much as 250 lbs of ascorbic acid crystals a month. (Editor's note: 250 lb/mo = 3700 g/day). That doesn't count pills. That's for a permanent population of 4 to 6 thousand. We have transients of course. Manufacturers think that Incline Village consumes more vitamin C per capita than any other place in the world.

Q. And no problems?

A. There is one aspect of which I think we should be wary: that's if the patient goes on high doses, 10-15 grams. He's usually the person who has hayfever or asthma or the like. After two to three years on these doses this patient will become dependent upon ascorbic acid; he'll get the feeling that he will get sick right away if he were to stop using ascorbic acid. Also, they frequently seem to get what are best described as sub-clinical infections that they have to take massive doses of vitamin C to block. This apparent dependence can usually be averted by giving the person high minerals and vitamins. What may be happening is that the vitamin C is chelating minerals and probably creating an additional need for other vitamins. Enemies of vitamin C might say that this is a reason not to take vitamin C. I think the solution is to take your minerals and vitamins.

You know there's another danger. If a patient who's accustomed to high vitamin C intake is hospitalized or otherwise comes under the care of certain physicians, the physician may cut off the C... and do it just when the patient needs it most.

Maintenance

Q. Now we're talking about maintenance. Until now it's been therapy; now we're into prophylaxis. One of the things I don't understand is why in vitamin C prophylaxis studies the controls never seem to be healthier than the treated group. That's clear in Coulehan's survey. He's always in the position of explaining why the superiority of the treated group appears to be insignificant—never the other way around. How much C do you take regularly?

A. I think that a person who has no really good reason to take vitamin C, no immediate illness, probably should do as Pauling says and take somewhere around 4 grams a day. People with allergies may find that they are more comfortable with higher amounts. I'm the last person in the world to maintain that you will never get a cold if you're taking maintenance doses of vitamin C. I get occasional colds. *But I can block the symptoms with vitamin C.* I never cease to be amazed at the number of patients that report to me that they used to get colds all the time and never get them since they take vitamin C. I don't know why the double blind study doesn't reflect this kind of subjective opinion.

I take 10 to 15 grams a day, first because I used to have hayfever. Vitamin C takes care of hayfever nicely in about two-thirds of all cases; and second, because there is evidence (14) that it reduces cholesterol and thus helps prevent arteriosclerosis, and third, I believe that vitamin C contributes to prevention of some cancers.

Q. What's your basis for the part about cancer?

A. What comes to mind immediately is work by Cameron in Scotland who has written with Pauling (15). They took 100 terminal cancer patients—terminal in that the chemotherapist, the radiotherapist, and the surgeons had no other treatments for them—put them on 10 g of vitamin C a day, and matched them with about 1000 untreated cancer patients. The worst results he got were in cases of cancer of the ovary. They lived only twice as long as the controls. Patients with cancer of the bowel lived seven times longer...

Q. And this is with what I can now call *only* 10 grams a day?

A. That's right. The overall average increase in survival exceeds fourfold, but this figure is going up all the time because all of the controls are dead, whereas a few, not many, but a few of the vitamin C patients are alive and without any sign of disease. I think that anyone with cancer should be taking high doses of vitamin C.

Now this experiment provides a therapeutic indication. It doesn't say much explicit about prevention. As far as a prophylaxis is concerned all I can say is that as a nutritionist I always seem to get at the cancer patients once everybody else has given up. Recently tests indicate that ascorbic acid does, indeed, reduce the amount of cancer in the bowels and I think that urologists have been using it in some cases of bladder cancer (16).

Q. So we have some 7000 patients with a variety of diseases whom you've treated over 10 years with vitamin C megadoses. Results have been uniformly good. No one has experienced a side effect that couldn't be reasonably handled. How come everybody isn't following you?

Science or sacred cow

A. That's not an easy question to answer. The answer has several parts. Part of the answer stems from the fact that experimentation that comprises the conventional wisdom, though honestly done, has been done on doses that are too small. Coulehan's review is a good illustration. In no way do I doubt the objectivity of his study or the sincerity of his conclusions. The problem is that he was using doses which are simply too small to mitigate symptoms. Let's go back to my custom of putting a number before a disease. The so-called common cold is caused by over a hundred different viruses so there are 20-gram colds, 50-, 100-, even 150-gram colds. It all depends on the toxicity of the particular case. Now if a person has a 20- to 30-gram cold, he has sniffles, he doesn't go to the doctor with that. Let's say he's read Pauling's book and decides to take 2 grams every hour. That rapidly eliminates the mild cold. Now see what happens. I'm sure that thousands of physicians have secretly read Pauling's book and decided that the next patient who comes in with a cold is going to get 2 grams every hour just like Pauling says. So the patient arrives at the office with a 100-gram cold. His throat is so sore that he thinks he has "strep;" he's aching all over and thinks he has the flu. His physician takes a culture and finds out by examination that he really has a bad cold. So he prescribes 2 grams of C an hour and nothing happens. To make something dramatic happen the physician would have had to use 100 or more grams. You just don't send a boy in to do a man's job.

Q. What you're saying is that the patient who has Pauling's 20-gram cold just isn't going to show up at the

Only what?

According to statistics compiled by the National Association of Insurance Commissioners, eliminating awards in excess of \$500,000 would reduce the sum total of all awards by only 6%, since few malpractice awards exceed \$500,000.

"What's more, according to testimony before Senator Edward M. Kennedy's Subcommittee on Health, only about 30% of the malpractice insurance premium dollar is paid to claimants. The rest stays with the insurance company or goes to pay administrative costs and legal fees.

"If the system is too expensive, it makes sense to see what can be done to reduce the 70% that constitutes the cost of running the system. All the haste, however, and most of the effort, seems to have gone into trying to squeeze down the 30% that goes to injured patients."

Consumer Reports, Sept. 1977

A matter of emphasis

"Emphasizing tort reform or insurance reform to the exclusion of medical reform is, putting the cart not merely before the horse but on top of it."

Consumer Reports, Sept. 1977

A second opinion

"No one doubts that large numbers of patients are killed and injured each year as a result of surgery that was unnecessary to begin with. In response to the problem (and as a way to control their own costs), some health-insurance companies have begun to pay for a "second opinion" on the desirability of surgery.

"Of course, the second doctor consulted can be wrong and the first one right. But the consensus is that obtaining a second opinion is a useful check on the need for a surgical procedure."

Consumer Reports, Oct. 1977

The Cathcart prosthesis

Q. Bob, tell me how your hip device came into being.

A. It's a modification of the Austin Moore device, a metal ball that fits inside the upper leg bone. It's used, for example, on the elderly person who falls and breaks the head of the thigh bone so that it has to be removed. The Austin Moore device was used for many years even though about a third of patients experienced a pain with erosion of the cartilage of the socket. Sometimes the ball would erode right through the socket. The Austin Moore ball is perfectly smooth and spherical, 41-47 mm in diameter. At first everyone thought that the metal was incompatible with cartilage, but that didn't prove to be the case, so the solution seemed to be to make the ball rounder and smoother. Now real bones didn't seem perfectly round to me, so at Stanford I measured 45 hips and found out exactly what the shape of the femoral head was and it wasn't round. I made some aspheric prostheses but didn't take the full 1 mm correction—just a little bit egg shaped—with the result that we have had no unexplained problems. There have been cases that have been infected . . . things like that . . . but the old problem of the prostheses just mysteriously sinking seems to stop. As a result the number of these units being used is increasing; it's now about 500 a month.

Q. Now any one who knows anything about mechanics knows that if you want a universal ball and socket you make it spherical; yet Nature made it egg shaped. Why?

A. Cartilage, which is porous, derives its nutrition from the synovial fluid. It's the "oil" within the joint. These irregular shapes pump this fluid through the porous cartilage, giving it its nutrition. A perfect sphere, no matter how you turn it, doesn't cause a pumping action. So in essence these out-of-round shapes create pumps. By the way, for your technologists I should point out that animal joints in a sliding friction situation have a coefficient of friction that's less than that of ice on ice, which is partially accomplished by this porous lubrication situation (17).

May 12, 1970

R. F. CATHCART III
JOINT PROSTHESIS

3,510,883

Filed Oct. 30, 1967
Superior

2 Sheets-Sheet 1

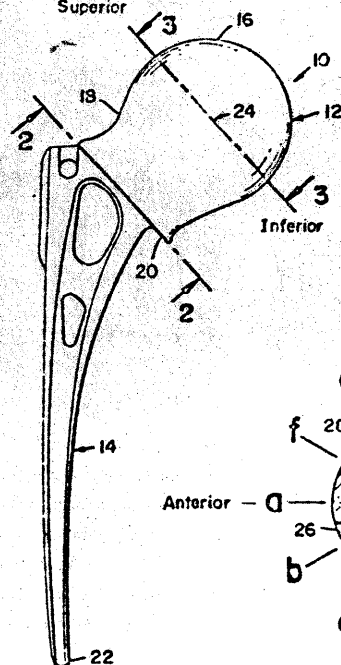


FIG_1

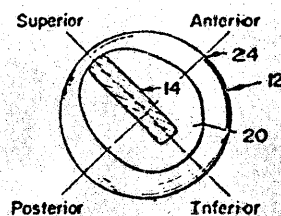


FIG_2

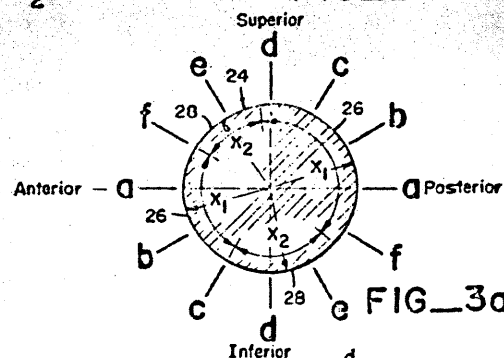


FIG_3a

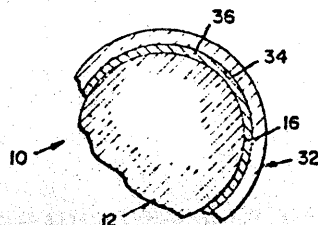


FIG_4

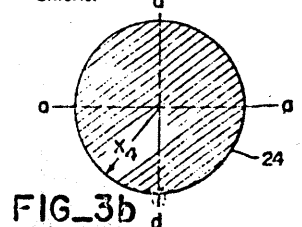


FIG_3b

INVENTOR
ROBERT F. CATHCART III
BY
Townsend and Townsend
ATTORNEYS

physician's office because people have learned that if you go to the doctor with a cold all he can tell you is take two aspirin and go to bed? Now you're saying that we should shoot at a cold with a 100-gram cannon. Well, if that's the case it seems to me that a plain, old fashioned, sensible double blind experiment ought to convince everyone. Right?

A. Well yes, but there are difficulties with that. I cannot conceive of how one could double blind these amounts of vitamin C. We are titrating between relief of malaise and onset of diarrhea. How can you find a double blind protocol to do that? You know we're all worshipping at the altar of double blind studies now. But obviously a reasonable person can tell for sure that something is working. In the first place I think we have to take account of this very interesting increased bowel tolerance which, of course, doesn't need a double blind study to prove. It demonstrates to anyone who has ever experienced it that something is going on that they just don't understand. But the result is certainly spectacular. Let's say you're testing a medication and get results that are, say, 40:60. Then you're going to have to double blind it. But if you hook up an IV and run a material in rapidly and within minutes you see that the symptoms of diseases are mitigated then



you really don't need a double blind. It would be very easy to take a hundred patients admitted with hepatitis to a large university center and give them ascorbic acid and compare them with the last hundred hepatitis patients that were admitted to that hospital. I think that the results would be convincing. The problem with double blind tests is that in a way you sometimes deceive yourself.

Q. Yes, I can almost see a group of patients each somehow identified as having a 100-gram cold. We split them. Give one group "C" and try to find something sufficiently sour to pass for vitamin C, which the patient can tolerate at 100 grams per day.

Have you published what you have done in the standard medical journals?

Why in CHEMTECH?

A. No, but I've tried. My manuscripts were rejected.

Q. What did the referees say? In chemical periodicals the editor refers the paper to referees he chooses, experts

in the field, and then forwards their comments, anonymously usually, to the author. Is that the practice in the medical periodicals?

A. In my case the manuscripts were just flat out refused.

Q. Just like that without any explanation?

A. Yes.

Q. Wow. Might it have something to do with an establishment protecting itself or something like that?

A. Well . . .

Q. Do you want to comment on this?

A. Well, really I don't. You know I really believe that the doctors involved in these decisions don't believe that this is true.

Q. In other words you think they're saying that this qualified physician who has an international reputation for his hip prosthesis has made all this up. Colds, flu, hepatitis, mono . . . , diseases a second-year medical student could recognize with high probability . . . they don't believe this?

A. Yup. They just don't believe it. They think I'm deceiving myself somehow. They see placebo effects as being very significant. I agree that placebo effects are significant, but I don't believe that they are *this* significant. Take the effects on children, on infants. In seven years I've not had to hospitalize a child who came in with a virus-induced fever.

Q. Wouldn't placebo effects be non-quantitative? If the physician gives the patient a couple of pills it won't make any difference whether he gives him big ones or little ones or two instead of four. How can we explain by placebo effect such a thing as a 50-gram cold and a 100-gram cold? It's the bowel telling you which you've got, not your head.

A. No question. This increased bowel tolerance is a spectacular phenomena that I wish all physicians could experience because once they experience it they know that something is going on.

Q. Is it conceivable that one can psychogenically control a case of diarrhea that normally appears at 10 grams and now all of a sudden when you're ill appears at 200 grams?

A. Oh there's no way that this can be psychogenic.

Q. And so we have, we have a problem here . . .

A. I think of communication.

Q. How do you feel about it?

A. Well, it worries me. It worries me in a lot of ways.

Q. The normal procedure in chemistry is if peers question a colleague's results, published or otherwise, they endeavor to repeat this work in their own laboratories. If they succeed they publish and if they don't succeed they publish. Doesn't that happen in medicine?

A. Well, understand first that this wasn't even published so people know of it only by word of mouth. One of the three physicians here in town is now using vitamin C for at least hepatitis cases. A fellow physician in Reno he's convinced to use it was amazed at the results. I treated an orthopedic surgeon in Carson City who had a serious case of hepatitis, and another in San Bruno who phoned because he knew of my work. Both these physicians are convinced beyond doubt that my megadose therapy altered the course of their hepatitis. But my work isn't widely known. I'm hoping that our chat will help, but it isn't easy to introduce new methods in medicine. It used to be that if a new physician came to town and he had

some new treatment then the senior physicians in the community would look at him, yes; but, because they had seen so much development in the past, it was a professional thing to stay out of this physician's way unless he showed that he was doing something really wrong. Competition would prove whether or not his ideas were right.

Malpractice!

Q. Patient would tell patient whether they believed this physician cured them or didn't?

A. Right. Now we're all living in a state of anxiety called the Malpractice Crisis. The first physician in town who does something new is not employing "practice of the community," and the last physician in town who adopts some procedure is also not employing "practice of the community." So there's a feeling that if we stop all progress, we will all get so practiced at "practice of the community" that we can't get sued anymore.

Q. "Practice of the community?" That's a legal term?

A. Yes, it's the criterion by which a physician is judged in court. Any change creates a debate within the medical community, which under ordinary circumstances is healthy, but now a change means that the "practice of the community" is in a state of flux so that attorneys for either side can get physicians for their side to testify that the defendant physician was or wasn't using "practice of the community." Take your pick.

Q. Do you have any idea how big a "community" the law uses in defining "practice of the community?"

A. I'm certainly not an expert on that, but as I understand it, it used to be more of a local community. Now it's getting to be more . . . almost an international community.

Q. International?

A. Yes, this creates a problem for us in rural medicine because when we're away from the large medical centers we don't have the facilities that they have in the big city. Sometimes we're forced to render care . . . don't have time to send them to the city . . . yet there can be criticism of the equipment that we have, for instance, and there can be a suit.

Now just because a suit is filed doesn't always mean that it's going to prevail, but defending a suit is a *misérable* experience for the physician. It puts him in a state of anxiety. The more idealistic he is—the more he used to care about patients—the worse it hurts him.

Q. And you've seen intensification in this. Seen it, for example, in what you pay for insurance. How has the premium changed over the years?

A. It went into a mad frenzy right after no-fault automobile insurance went into effect. Attorneys didn't seem to have anything to do so they launched a campaign against physicians. When I started practice I paid about

\$800 a year for insurance. That was in 1969. I quit surgery because of the whole malpractice thing three, four years ago, when the jump was from \$4000 to \$8000. In some cases insurance now costs \$20 000 to \$30 000 for an orthopedic surgeon.

There's an interesting paradox here: the more surgery a person does, the more insignificant a large malpractice premium becomes in his overhead. So a surgeon who tries to avoid doing surgery is the one who's kicked out of the surgical field first. I know a fellow in San Francisco who does, oh maybe 100, 150 laminectomies a year . . . that's back surgery, disk removal. Anyway, some people do a lot of laminectomies but the frequent need for them is a debatable point in orthopedics. So what happens? Those of us who feel that fewer should be done are in a sense being taken out of competition by the malpractice crisis.

Q. Are you saying that a physician who is doing this kind of surgery is going to pay, say, \$30 000 a year for insurance no matter how many such operations he performs? For our friend who does 150 operations a year—3 a week—that's \$200 per case just for insurance. It's obvious what happens if he talks himself out of doing half of those.

What kind of patient do you most often find involved in malpractice suits?

A. First he's a patient with the more serious kind of problem, so that means that the more specialized a physician is, which means often the more competent he is, the more likely he is to get sued. The neurosurgeon, the cardiovascular surgeon . . . they get sued the most because they take on the most responsibility. The orthopedic surgeon gets sued a lot not only because he handles difficult problems, but also because many of his patients have had accidents, so their cases are automatically reviewed by attorneys. It's interesting that the doctor who avoids serious problems is perhaps less of a scientist, less up on his work, concentrates on simple things, has a good personality, relates well with his patients. He's less likely to get sued.

Q. Is he the one who sets the "practice of the community," not deviating not doing anything new?

A. That's right. Whereas the highly skilled person who may be a little introverted . . . that's the only reason he can stand to be that skilled . . . has to go to class a lot, spend his life studying, not watching football games, drinking beer Saturday night . . .

Q. Reading a lot of journals?

A. Yeah, so that this fellow may not have the personality but he's the specialist and he's more likely to get sued.

Q. Fair enough. But maybe tonight we can break that lock step. Let me buy you a beer before we call it a night.

A. OK, and I can tell you about the hip prosthesis I developed. I don't have hours *that* early tomorrow . . .

EPILOGUE

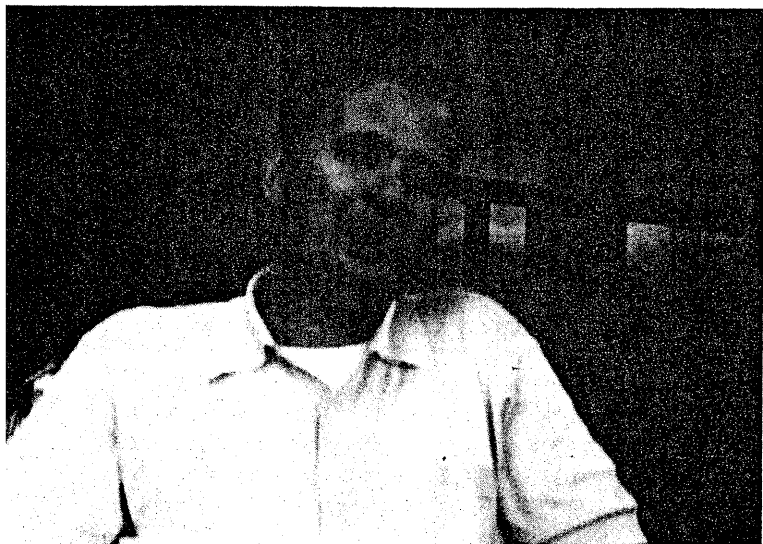
It's amazing, sometimes, to what extent an Editor will go to assure the quality of his publication! Like in this case—I went out and caught the flu. Wednesday evening I realized my scratchy throat had gotten worse and I ached, so after dinner, I added two more grams of ascorbic acid to the four I'd already taken that day. By 10 my fever was a bit over 101° so I took another 3 grams, which seemed like a lot, and went to bed. I probably should have continued popping pills all night 'cause next day I woke up achy with my temperature already a degree above normal. I im-

mediately started a vitamin C regime of 4 g per hour; by 11 my temperature was down and I felt fine. That afternoon, with my pocket full of gram-size pills I attended a Board meeting, an open house (SIPI), a dinner of the Research Directors Association, walked briskly about 2 miles to and from the train and tumbled into bed, tired but symptomless. I'd kept up a steady 2 g/h all afternoon so my daily take was 44 g.

That night I didn't sleep very well: I must have groped to the john a half dozen times. (Dr. Cathcart did warn me

of that. Said he, "I even got blamed for an apparent increase in Incline Village's population." "Oh, does C do *that*, too?" "No, but they use a T.V. toilet-flush index to estimate population and in the flu season in Incline Village it goes up.")

On my 2:00 a.m. return trip I started medication so that by wake-up at 7:30 I had 15 g in me already . . . and a low fever. I upped the dose to 5 g/h and then at noon to 6 g/h. That's equivalent to 144 g/24 h day. That calculation convinced me that I must be really sick, though I felt fine—well, not absolutely. I had finally gotten close



enough to bowel tolerance to have developed a fine case of *magensprache* (literally, stomach speaking); and was so flatulent I felt like the Hindenberg reincarnated. Anyway, having convinced myself that I was really ill, I phoned Dr. Cathcart.

"Yes, at that dosage you're close to something that would put you in the hospital if you weren't on ascorbic acid at bowel tolerance."

"Yes, take it every hour; No, a 6 g dose isn't too much. My experience is more with powder than pills but I've used a single dose of 2 tablespoons of powder in water for mono." (That's about 25 grams)

"You could use a controlled release formulation at night."

"Oh, I'd *certainly* see your physician. You could have something bacterial on top of the virus. He may want to do a culture. *Do* see him."

"Yes, you *are* contagious but at least you're not sneezing all over everyone."

So, off I went to my internist and tried to explain to him why I was there without any symptoms.

"Oh, you have something; throat's red. No need to culture it now. Just take it easy for 5 days. If you want to take all that vitamin C, go ahead. It'll just come out in your kidney; probably can't do any harm. Just don't get a lab test for gout. I've seen a lot of false uric acid positives since Pauling started everyone on ascorbic acid."

"But couldn't I have something terrible that the C is masking? It takes all the symptoms away."

"I can do that with aspirin. Call me if anything comes up. You're vulnerable even if you feel good."

Saturday, day three, I took it easy. Also I took about 75 g of C. I didn't keep track. By then I was popping 1000 mg pills like bar peanuts.

Sunday I spent in the office. At 30 g in four hours I found out what happens if you exceed bowel tolerance. No big deal. The rest of the day I felt fine and took no more pills 'til it was time for dinner and the theater. Then I popped a 5 g "prophylaxis".

Monday, day five, I decided to see if I was well: I took "only" 4 g and waited to stop aching and sneezing. By noon I was functional but mildly miserable so I tried my physician's aspirin routine. It didn't help much. But a 5 g dose of C at 3:00 p.m. and another at 4:00 had me feeling fine—just a bit gassy.

By Thursday, day eight, I had morning catarrh, more severe than usual, a throat tickle that came and went, and four empty, 100 g, vitamin C bottles.

Friday found me fine on 4 g maintenance.

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Symptomectomy

A chat with Robert Cathcart, M.D.

B. J. Luberoff

Incline Village, Nevada, is a community of 5000 souls, more or less, except during skiing season. Then it swells beyond 15 000. It's on the North shore of Lake Tahoe. a beautiful hour's drive over Mt. Rose from Reno.

Make believe that you're there, sitting in the living room of the 5000 square foot lakeshore home designed by Robert Fulton Cathcart, III, M.D. There's a fire crackling in his wall to wall, floor to ceiling stone fireplace. The first thing you might want to ask him is how in the world he came to practice medicine in Incline Village? Did it have anything to do with his being an orthopedic surgeon and how some people ski?

Well I had the chance to spend such an evening with Bob Cathcart and to ask him that question, and some others. Here's how it went.

A. Orthopedics isn't what really brought me here. I had practiced five years in San Mateo—that's on the San Francisco peninsula. During that period I invented and patented what's now a widely-used hip prosthesis ... we can talk about it later ... but then I became interested in nutrition, specifically vitamin C. After reading Pauling and everything else I could on the subject, I started "experimenting" with vitamin C first on myself and the family and then on a few selected patients. I made some basic discoveries, and it's them I really want to tell you about.

Now in San Mateo I had little opportunity to treat patients with vitamin C. Peer pressure at that time, about seven years ago, was pretty much against the physician using vitamin C. Besides, as an orthopedic surgeon, in a region where specialization was respected, I seldom saw patients who had colds, or other viral diseases. So I commuted to Incline Village every week for a year. It's only a few hours' from San Francisco. Here I went into association with a general practitioner who planned to go to another town after about a year. During that year I demonstrated that *properly used*, vitamin C could decrease most of the morbidity and all of the mortality from viral diseases. I contacted Pauling about this and he said that he knew of no other physician who was doing exactly what I was doing.

Q. What was that?

A. Well first let me give you some background. Fred Klenner of Reidsville (*1*), North Carolina, one of the greats in vitamin C therapy, has been working with it for what seems like twenty or thirty years. He found that he could detoxify most virus diseases with intravenous doses of "C". Now he even uses it for carbon monoxide poisoning, barbiturate poisoning, even snake bites. Now what I discovered, which was different, is this: the average person, at least 80% of normal individuals, when they are well can take, orally, between 10 and 15 grams of vitamin C, in divided doses, during the day before—

Q. Hold on, did you say 10 to 15 *grams*?

A. That's correct, 10 to 15 *thousand* milligrams a day. Most people can take that much before it produces diarrhea. Some people can tolerate less, a few can take more ... *when they're well*. The astonishing thing is that this same person ... the patient who when well gets diarrhea on say 12 grams ... when ill with a moderate cold can take 30 to 60 grams without diarrhea; with a bad cold or a flu, 100 grams, sometimes even 150 grams, and with viral diseases such as mononucleosis or viral pneumonias, I've used in excess of 200 grams a day without it producing diarrhea...

Q. That's nearly a half pound ...

A. That's correct. In some cases the body evidently

with vitamin C

needs that much, albeit for only a short time. With mononucleosis or viral pneumonias, during the first couple days of the disease we sometimes see a need for that half pound—more or less. Patients with bacterial diseases will absorb similar amounts depending on level of toxicity. Of course, they should get the appropriate antibiotic, too. Essentially, the sicker you are the more you can take; and taking enough—and *that's important*—seems to detoxify you. You get well quickly. And as you do you find that you can tolerate less and less ascorbic acid until you go back to normal when you're well.

Now there's been a lot of talk about double blind studies and about the benefits of vitamin C in preventing colds and things like that. Your article by Coulehan (2) is a case in point...

Q. Let me slow you down just a minute. What you're saying is that an average, healthy person can take about 10 grams a day. If he's well and takes much more he'll begin to feel malaise in the gastrointestinal system, and if he persists he'll get diarrhea.

A. Right.

Q. But if he has a viral illness then he can take a lot more, and doing so will make him feel very much better, very fast. What's this saying about what is happening in the GI system and elsewhere?

A. Well, we think that ingested vitamin C in the GI system is in equilibrium, you might say, with that in the bloodstream. It's absorbed through the stomach and the intestines into the blood stream to maintain some kind of "saturation" there. Now if, for whatever purpose, the blood is "throwing off the vitamin C at a high rate, then more and more will be absorbed so that the vitamin C in the intestine does not reach the rectum. If it does in sufficient amount to create a hypertonic situation, then body fluids migrate to dilute it and that produces mild diarrhea.

Our genetic defect

Q. So you kind of "titrate" the illness. But if the body really needed all that ascorbic acid, wouldn't it just make it?

A. Ah, that's the point—it *can't*. Irwin Stone (3) and others say that man has some sort of genetic defect, that in the evolutionary process the higher primates lost the ability to synthesize ascorbic acid. Only a few other animals share this "defect": the guinea pig and an African fruit-eating bat and some minor species. By and large the lower animals synthesize ascorbic acid in the kidneys; higher up the evolutionary tree, they make it in the liver. It really is a liver metabolite in higher animals. Now how did this happen? Well, the higher primates evolved in areas that had fruits and vegetables in profusion. Just think of the monkey sitting around eating bananas and

leafy things that have a lot of ascorbic acid. He was fit enough to survive in this environment. The stresses on him were not great. He was not exposed to as many infectious diseases as we are. So the ability to synthesize vitamin C offered little survival value and was lost. Now along came man with his great capability and curiosity, and he ventured out from these Gardens of Eden and went into areas where food ascorbic acid was scarce. His diet changed. The biggest change came when he went out on the sea. There, without any fruits and vegetables, he got scurvy, that's the acute deprivation of vitamin C. It was only when the British discovered that lime juice could prevent scurvy (8) that men were able to go for long distances out on the sea. Scurvy will be induced in two to three months if you're on a completely vitamin C free diet. Then you'll start manifesting symptoms of the disease and without treatment you'll die in another month or so. But preceding the scurvy syndrome are a variety of low blood ascorbic acid states. Stone and Pauling popularized them and pointed out that they lead to various diseases from which mankind suffers.

Q. What does ascorbic acid do normally?

A. The non-controversial functions of ascorbic acid (4-6) include several enzymatic processes, the body's ability to make collagen, dentine, adrenalin, corticoste-

roids, maintain proper functioning of the immune system, the blood coagulation system, metabolism of several amino acids. Lewin (7) believes that ascorbate aids in formation of cyclic AMP and inhibits its hydrolysis which, if true, means that vitamin C indirectly affects almost every hormone function ...

Q. That's quite a spectrum of different kinds of activity.

A. That's right, and everyone agrees on the need of ascorbic acid here. The quarrel is over how much is needed for these functions. When someone is well, the amount needed may be small. But what happens when he's ill? What attracted me is that if someone dies suddenly; say has been killed instantly in an automobile accident, then his tissues contain a lot of ascorbic acid. (The adrenal glands have the highest concentration.) However, when

a person dies after an illness, the body contains almost no ascorbic acid.

Now isn't it striking how many people who have been admitted to the hospital with one disease get phlebitis, or a heart attack, or a stroke, all disorders of the vitamin C sensitive blood clotting system? Or they get pneumonia, a disorder of the immune system. How many illnesses seem to occur after a period of physical stress, after some previous disease, viral, bacterial? There's even been work that relates emotional stress to physical disease. Well, it just figures that if we see some chemical run down under stress we ought to try to replace it.

Q. Fair enough—but how much do you need? How much, for instance, do other animals make? Well ones.

A. The goat is often taken as a reference point because he weighs about the same as a person.

Q. And because he, too, eats a capricious diet?

A. Well... no... anyway a 70-kilogram goat will make about 13 grams of vitamin C a day.

Q. In light of that, the numbers you mention, 10 to 15 grams for a healthy adult human, is not totally inconceivable. How about other models?

A. Several other animals have been assayed. These are ballpark figures for most of them. Cats and dogs make ascorbic acid, but perhaps they can't always make as much as might be ideal so they suffer from such toxic diseases as distemper. A veterinarian in San Jose has been curing distemper with ascorbic acid injections (9).

Isn't it interesting, when you reflect on it, that the guinea pig, who can't make vitamin C, is a generally accepted model for testing human diseases? I've often said, tongue-in-cheek of course, that if you've got a disease you can't give to anything but man, monkey, and guinea pig, you've got a sure bet that you can cure it with vitamin C.

Clinical insight

Q. OK, let's go back to curing things. You referred me to Lewin's new book (7). It's very thorough and goes to great length in its discussions of modes and mechanisms of action and metabolic pathways and so forth. As a biochemist that's about all Lewin can do. Now we may not understand how the body is doing whatever it's doing, but people will get sick and have to be treated. You approached things pragmatically. You treat patients. Tell us about that.

A. My practice is to let the body take as much vitamin C as it needs ... take an amount proportional to the amount of toxin that's around. Remember, everyone else has been talking about a *fixed* dose, usually at what I consider to be only a homeopathic level. Their studies go from 2 to maybe 4 grams a day and they see little clinical effect and none statistically. That doesn't surprise me. Such doses simply do not take on a disease after it's established. So that if you have a 100-gram cold ... it's my custom to put a number before the name of a disease to represent the amount of vitamin C which that patient can consume the first couple of days of the disease without diarrhea ... so that if you have a 100-gram cold and the patient is taking roughly 100 grams a day, you will quickly eliminate perhaps 90% of the symptoms of the disease. But if you treat that same cold with 2 grams or even 20 grams a day you won't see much happen. In some cases, especially if treated early, it almost seems as if megadoses were killing viruses.

With bad colds or influenza we don't seem to shorten

the duration of the infection, but we render patients sufficiently asymptomatic so that they weather the infection without complications. Most of the time my patients don't have to miss any work time. If you're using enough ascorbic acid it will promptly take a fever down to normal, and you won't have the normal aches and pains of flu-like diseases.

Q. So we're talking about treatment versus prevention. That seems a little hard to demonstrate in a normal double blind experiment: the dose has to be tailored to the individual's disease and to its stage. Before we look further at that problem—and it's a real one—let me ask you to share more of your clinical experiences.

Pneumonia

A. Let me give you a typical case, a lady here, about, oh, 28, developed viral pneumonia. As far as I could tell she did not respond to antibiotics and she never did "culture" any place. When she presented herself she was very ill, high temperature, the right upper lobe infiltrated with the pneumonia process; difficulty breathing. So we hooked her up to intravenous ascorbic acid, about 1 gram per 18 cc's, and ran it in just as fast as we could. I gave her about 55 grams by vein and the remainder orally, about 215 grams went into her between 11 o'clock in the morning and 9 o'clock that night, at which time the pneumonia went into crisis. She drenched three sets of bed clothing that night. The next morning she was feeling much better. We did the same thing the next day. She returned to work less than a week after I first saw her. We have daily x-rays that demonstrate the rapid dissolution of the pneumonia process.

At that time I treated two other people in town who had the same thing, and got similar results. Three other patients in town went to other physicians and were hospitalized about two weeks and weren't much better when they came out.

Q. I'm sure a lot of scientists will say "Well that's just anecdotal...." To me it seems that when we don't know how a therapy works or can't demonstrate efficacy in a rigid protocol, then we have to rely on individual clinical experience.

You'll recall that I first contacted you because I suspected that vitamin C might have some value in treating my son's mononucleosis, a very debilitating disease particularly common among students. It knocked my son out for the entire summer and we were told that it has no treatment, other than lots of rest. Can you do anything with mono?

Mono

A. The first patient that I ran into with it was a junior high school librarian who was about 22 and weighed about 100 pounds wringing wet. She came in with a severe case of mononucleosis. I told her about the bowel tolerance idea and explained to her how to do this self-titration. I saw her three or four days later; she was almost completely well.

Q. This lady really had mono?

A. Oh yes. Mononucleosis is a disease we can spot without a tremendous amount of lab work. Usually you do a heterophile test and look at the white cells. A positive is quite definitive; a negative can be misleading.

The typical patient who gets mononucleosis is exactly

the one who does the best on vitamin C: older teenagers or young adults are just fantastic vitamin C takers. They can understand the bowel tolerance idea, have iron stomachs, and couldn't care less about slight gas and diarrhea when they have this horrible disease ... In fact the sicker a patient is the better he does because the relief of symptoms is so dramatic that they don't need any arguments to convince them to continue treatment. So what usually happens is that in three to five days the symptoms are 90% relieved. Then some get the message loud and clear: if they stop the vitamin C too soon they get sick all over again.

The infection may go on just about as long as it would have in the first place, but the person is functional and doesn't develop complications. He can go back to school or work or whatever. But he must continue to take vitamin C doses as high as the bowel will tolerate. It can be many months, sometimes a year, before he's down to a normal 10-15 grams per day. He just titrates between relief of most symptoms and diarrhea. The titer will decrease from day to day unless he stops taking the vitamin C. Then there's a resurgence of the disease, and you go up to higher doses again and bring it back down.

The important thing with mono or other responsive dis-

eases is that we can get people back to work in days. You know we're in ski country here. I would be unhappy if one of my ski patrols wasn't back on duty within a week or ten days after having contracted mononucleosis.

Q. This is a disease that has a unique, positive diagnosis, so it's not possible that we're seeing some kind of artifact. You're sure that you're seeing mono?

Hepatitis

A. Oh, sure. The other disease that is very specific is infectious hepatitis. Let me tell you about it. It's a cinch for vitamin C. The difference between the course of the disease with and without vitamin C is quite obvious if only because hepatitis is a disease that we can put numbers on. There are various enzyme systems that we can follow to

show the course of the disease. Infectious hepatitis can be mild where the patient is just a little yellow and maybe a bit tender in the abdomen, but not very sick. But the patients I'm talking about—20 of them, at least—were profoundly ill with hepatitis, and here again we were able to detoxify them in three to five days. The patient is feeling essentially well in three to four days. It generally takes about six days for the jaundice to clear. In two to three days the urine returns to normal color. (You see, with hepatitis the bile is blocked in the liver so that the urine turns brown and the stool turns clay white.)

Hepatitis is a serious problem following blood transfusions. As a matter of fact the whole system of gathering blood in this country is undergoing revision because people who sell their blood have a high incidence of hepatitis. That's why they're trying to go completely to a voluntary system. I'm not sure that's necessary because it's apparently so simple to control hepatitis: just give patients vitamin C after blood transfusions. One Japanese physician (10) has shown that his patients don't get hepatitis if he puts them on maintenance doses of ascorbic acid following blood transfusions. Anybody who is stressed enough to need a blood transfusion should be getting large doses of vitamin C anyway.

Psychoactivity

Q. You use the term stress. To the layman that means psychological stress. Do you mean to imply that vitamin C has any benefit in that kind of situation?

A. I've been using the term stress in its broadest medical sense, but the average person under mental stress can often take a few grams more than he could ordinarily tolerate. Patients who do, say that they feel better and subjectively think that they can meet the stress better.

Vitamin C is definitely psychoactive (11). Schizophrenic patients require 10 times as much vitamin C as others to develop the same ascorbic acid level in their urine.

A Dr. Libby (12) in Los Angeles discovered that ascorbic acid or sodium ascorbate, I think he uses about 60 grams a day, can detoxify heroin addicts almost immediately. (He administers a protein extract with the "C" because he found heroin addicts to be low in proteins.) I had a little experience in this but didn't have enough patients here to follow up on it. Libby practices near a Methadone Center. He found that on his program, patients get no effect from the fix. If they take their 60 grams of sodium ascorbate they can do the heroin and it has no effect whatsoever; later they find they have no withdrawal symptoms, and soon give it up. Heroin addicts mostly want to give up their addiction, but previously all they had was a choice between feeling rotten and feeling horrible.

You know, Stone feels that there is a receptor site in the brain that would be filled by ascorbic acid if there were enough (12). But instead that site is filled with such things as heroin or morphine or barbituates. One end of the molecule fits in where ascorbic acid ought to fit but the other end sticks out and that's what does the crazy thing. Well, if you give ascorbic acid, it displaces the unwanted molecule and also blocks the need for it, so no withdrawal symptoms.

Side effects

Physicians have difficulty in thinking of something that does so many different things. We're used to medicines

that are fairly specific. Now ascorbic acid has these myriad, noncontroversial functions that go on in many many different systems of the body. Essentially what I found is that by giving huge amounts of ascorbic acid, it would tune up, if you will, all of these functions to high efficiency, far more than what's been experienced with the lower doses. Some of the enemies of ascorbic acid point out that there is no ascorbic acid in the body when a person is sick, yet he gets well anyway. They say that proves that you don't need ascorbic acid. It's like recommending that a football coach hold his first team on the bench because he's just barely winning with his second team.

Q. OK. So with all that we must come around to why this megadose therapy isn't widely used. The first thing that comes to mind is that it must have some absolutely terrible side effects. What would you say is the worst side effect other than diarrhea that ascorbic acid produces?

A. Well some people don't like the taste.

Q. And that you call a terrible side effect?

A. Certain patients feel they have trouble with acids in general. They are usually nonspecific about it and have avoided oranges, lemons, grapefruit, and things like that all their lives. These people frequently have a lot of difficulties late in life, I think because they're unusually low in vitamin C. Some patients do indeed have difficulties in first taking ascorbic acid.

Q. How about sodium ascorbate?

A. I've been reluctant to use large amounts of sodium ascorbate—that's a friendly differences between Stone and me. Stone feels that the problems people get into when they take large amounts of sodium could be avoided by taking sodium ascorbate. For instance the hypertensive, who shouldn't eat large amounts of sodium, wouldn't have been hypertensive in the first place if he or she had taken large amounts of ascorbic acid all his life. Well that may be true, but when I see a patient with an acute viral disease I don't want to flood his system with sodium. Imagine how much sodium is needed to neutralize 200 grams of ascorbic acid. So I use the free acid. One in a couple thousand may break out in a rash about the face or soft parts. This is transient and, usually, if they persist in their vitamin C regime, it goes away.

Many people who are intolerant to vitamin C by mouth become tolerant after a few days on intravenous vitamin C. I've never found a person who was intolerant to vitamin C injections.

People who have ulcers sometimes don't tolerate ascorbic acid. Interestingly half the people with ulcers swear that they get well with vitamin C and the other half say they get worse. I'm not entirely sure why that is.

Q. How about kidney stones?

A. I've never seen an oxalate kidney stone among my regular vitamin C takers. There is a theory that says that ascorbic acid breaks down to oxalate so that if a person had difficulty handling oxalate he could precipitate oxalate stones. But the situation is paradoxical: I'll grant that if a person did have difficulty handling oxalates, and he took maybe 500 mg of ascorbic acid a day, he might increase his oxalate load, but the paradox is that if a person takes the powder in large doses, as large as I've been talking about, it somehow makes the oxalate more soluble in the urine. (Ed: Cation chelation?) Anyway, the pragmatic fact is that in my experience oxalate stones caused by vitamin C are not something to worry about.

I have had four patients complain that they had some

Cathcart on malpractice

Now that I have a house and a family and so many responsibilities I wouldn't dream of trying to apply this technology in view of the present malpractice crisis.

If the Federal Government would lay off and consumer advocates understand health care delivery, then market pressures would rapidly bring into being things people need. All the do-gooders, the people who would like to protect us from malpractice, are doing the exact opposite of what they set out to do and they're doing it in a big way. Technological advance renders malpractice and incompetence almost insignificant. Today the least competent doctor can prevent polio better than the best physician could treat it 30 years ago. Studies on ascorbic acid that I was starting with post-operative patients just as I quit surgery were yielding results which, if pursued, probably would have alone decreased the annual morbidity from surgery far more than all of the morbidity involved in malpractice suits in a year in the United States. But we're afraid of new things and as long as we are we're not going to get them. This fear retardation accumulates like compound interest. Research accumulates like compound interest; it builds on itself. If something new is delayed we're stuck with that delay forever. The amount of human suffering for the remainder of history of mankind caused by unreasonable fear retardation, by this loss of compounding of interest in clinical research, means that we are causing astronomical amounts of human suffering.

burning sensation on urinating when they took large doses of ascorbic acid, but I've certainly never seen anything like the report that came out shortly after Pauling's book that in Europe, where they use ascorbic acid in the treatment of tuberculosis, that screaming could be heard from the sanatorium men's room. My experience with this is vast and I can say without qualification that that story is an absolute lie. It does not happen. The other thing that has been said is based on a study by Victor Herbert (13) that indicated that vitamin C blocked vitamin B-12 metabolism. This was front page news; but I understand that other studies indicate that there were some difficulties with his tests *in vitro* and that, indeed, this does not happen in humans. In any event, I have never seen any evidence of B-12 blockage or pernicious anemia. As a matter

of fact our patients seem to have pretty thick blood. Of course we're here at high altitude so we could expect that.

In summary then, I find no difficulty whatsoever, except those minor things I've mentioned.

Q. No side effects. Doctor, to how many patients would you estimate you've given megadoses of vitamin C?

A. I think it's been about 7000 patients over the last 10 years. During epidemics in my village, the local pharmacies have sold as much as 250 lbs of ascorbic acid crystals a month. (Editor's note: 250 lb/mo = 3700 g/day). That doesn't count pills. That's for a permanent population of 4 to 6 thousand. We have transients of course. Manufacturers think that Incline Village consumes more vitamin C per capita than any other place in the world.

Q. And no problems?

A. There is one aspect of which I think we should be wary: that's if the patient goes on high doses, 10-15 grams. He's usually the person who has hayfever or asthma or the like. After two to three years on these doses this patient will become dependent upon ascorbic acid; he'll get the feeling that he will get sick right away if he were to stop using ascorbic acid. Also, they frequently seem to get what are best described as sub-clinical infections that they have to take massive doses of vitamin C to block. This apparent dependence can usually be averted by giving the person high minerals and vitamins. What may be happening is that the vitamin C is chelating minerals and probably creating an additional need for other vitamins. Enemies of vitamin C might say that this is a reason not to take vitamin C. I think the solution is to take your minerals and vitamins.

You know there's another danger. If a patient who's accustomed to high vitamin C intake is hospitalized or otherwise comes under the care of certain physicians, the physician may cut off the C ... and do it just when the patient needs it most.

Maintenance

Q. Now we're talking about maintenance. Until now it's been therapy; now we're into prophylaxis. One of the things I don't understand is why in vitamin C prophylaxis studies the controls never seem to be healthier than the treated group. That's clear in Coulehan's survey. He's always in the position of explaining why the superiority of the treated group appears to be insignificant—never the other way around. How much C do you take regularly?

A. I think that a person who has no really good reason to take vitamin C, no immediate illness, probably should do as Pauling says and take somewhere around 4 grams a day. People with allergies may find that they are more comfortable with higher amounts. I'm the last person in the world to maintain that you will never get a cold if you're taking maintenance doses of vitamin C. I get occasional colds. *But I can block the symptoms with vitamin C.* I never cease to be amazed at the number of patients that report to me that they used to get colds all the time and never get them since they take vitamin C. I don't know why the double blind study doesn't reflect this kind of subjective opinion.

I take 10 to 15 grams a day, first because I used to have hayfever. Vitamin C takes care of hayfever nicely in about two-thirds of all cases; and second, because there is evidence (14) that it reduces cholesterol and thus helps prevent arteriosclerosis, and third, I believe that vitamin C contributes to prevention of some cancers.

Q. What's your basis for the part about cancer?

A. What comes to mind immediately is work by Cameron in Scotland who has written with Pauling (15). They took 100 terminal cancer patients—terminal in that the chemotherapist, the radiotherapist, and the surgeons had no other treatments for them—put them on 10 g of vitamin C a day, and matched them with about 1000 untreated cancer patients. The worst results he got were in cases of cancer of the ovary. They lived only twice as long as the controls. Patients with cancer of the bowel lived seven times longer ...

Q. And this is with what I can now call *only* 10 grams a day?

A. That's right. The overall average increase in survival exceeds fourfold, but this figure is going up all the time because all of the controls are dead, whereas a few, not many, but a few of the vitamin C patients are alive and without any sign of disease. I think that anyone with cancer should be taking high doses of vitamin C.

Now this experiment provides a therapeutic indication. It doesn't say much explicit about prevention. As far as a prophylaxis is concerned all I can say is that as a nutritionist I always seem to get at the cancer patients once everybody else has given up. Recently tests indicate that ascorbic acid does, indeed, reduce the amount of cancer in the bowels and I think that urologists have been using it in some cases of bladder cancer (16).

Q. So we have some 7000 patients with a variety of diseases whom you've treated over 10 years with vitamin C megadoses. Results have been uniformly good. No one has experienced a side effect that couldn't be reasonably handled. How come everybody isn't following you?

Science or sacred cow

A. That's not an easy question to answer. The answer has several parts. Part of the answer stems from the fact that experimentation that comprises the conventional wisdom, though honestly done, has been done on doses that are too small. Coulehan's review is a good illustration. In no way do I doubt the objectivity of his study or the sincerity of his conclusions. The problem is that he was using doses which are simply too small to mitigate symptoms. Let's go back to my custom of putting a number before a disease. The so-called common cold is caused by over a hundred different viruses so there are 20-gram colds, 50-, 100-, even 150-gram colds. It all depends on the toxicity of the particular case. Now if a person has a 20- to 30-gram cold, he has sniffles, he doesn't go to the doctor with that. Let's say he's read Pauling's book and decides to take 2 grams every hour. That rapidly eliminates the mild cold. Now see what happens. I'm sure that thousands of physicians have secretly read Pauling's book and decided that the next patient who comes in with a cold is going to get 2 grams every hour just like Pauling says. So the patient arrives at the office with a 100-gram cold. His throat is so sore that he thinks he has "strep;" he's aching all over and thinks he has the flu. His physician takes a culture and finds out by examination that he really has a bad cold. So he prescribes 2 grams of C an hour and nothing happens. To make something dramatic happen the physician would have had to use 100 or more grams. You just don't send a boy in to do a man's job.

Q. What you're saying is that the patient who has Pauling's 20-gram cold just isn't going to show up at the

The Cathcart prosthesis

Q. Bob, tell me how your hip device came into being.

A. It's a modification of the Austin Moore device, a metal ball that fits inside the upper leg bone. It's used, for example, on the elderly person who falls and breaks the head of the thigh bone so that it has to be removed. The Austin Moore device was used for many years even though about a third of patients experienced a pain with erosion of the cartilage of the socket. Sometimes the ball would erode right through the socket. The Austin Moore ball is perfectly smooth and spherical, 41-47 mm in diameter. At first everyone thought that the metal was incompatible with cartilage, but that didn't prove to be the case, so the solution seemed to be to make the ball rounder and smoother. Now real bones didn't seem perfectly round to me, so at Stanford I measured 45 hips and found out exactly what the shape of the femoral head was and it wasn't round. I made some aspheric prostheses but didn't take the full 1 mm correction—just a little bit egg shaped—with the result that we have had no unexplained problems. There have been cases that have been infected ... things like that... but the old problem of the prostheses just mysteriously sinking seems to stop. As a result the number of these units being used is increasing; it's now about 500 a month.

Q. Now any one who knows anything about mechanics knows that if you want a universal ball and socket you make it spherical; yet Nature made it egg shaped. Why?

A. Cartilage, which is porous, derives its nutrition from the synovial fluid. It's the "oil" within the joint. These irregular shapes pump this fluid through the porous cartilage, giving it its nutrition. A perfect sphere, no matter how you turn it, doesn't cause a pumping action. So in essence these out-of-round shapes create pumps. By the way, for your technologists I should point out that animal joints in a sliding friction situation have a coefficient of friction that's less than that of ice on ice, which is partially accomplished by this porous lubrication situation (17).

May 12, 1970

R. F. CATHCART III
JOINT PROSTHESIS

3,510,883

Filed Oct. 30, 1967
Superior

2 Sheets-Sheet 1

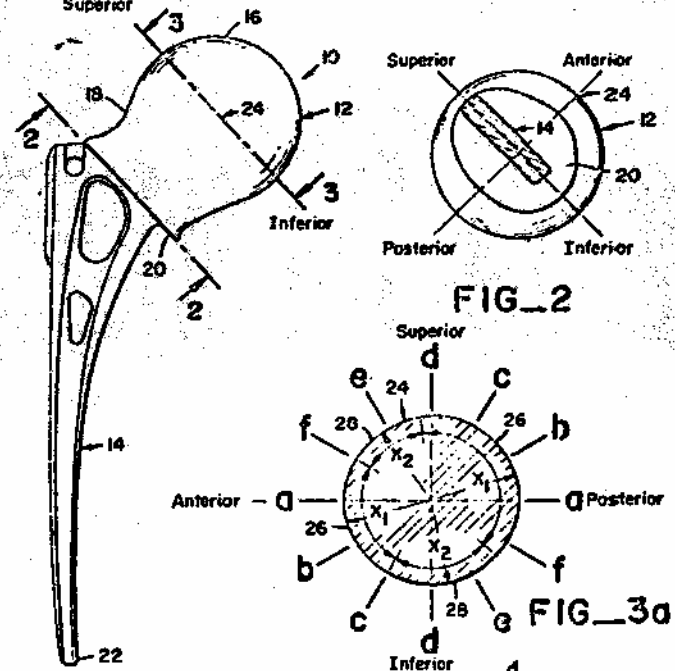


FIG_1

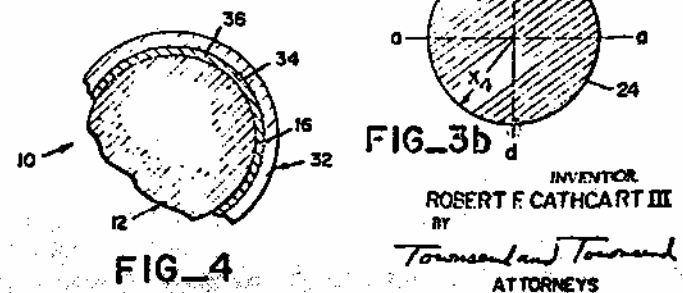


FIG_4

INVENTOR
ROBERT F. CATHCART III
BY
Townsend and Townsend
ATTORNEYS

physician's office because people have learned that if you go to the doctor with a cold all he can tell you is take two aspirin and go to bed? Now you're saying that we should shoot at a cold with a 100-gram cannon. Well, if that's the case it seems to me that a plain, old fashioned, sensible double blind experiment ought to convince everyone. Right?

A. Well yes, but there are difficulties with that. I cannot conceive of how one could double blind these amounts of vitamin C. We are titrating between relief of malaise and onset of diarrhea. How can you find a double blind protocol to do that? You know we're all worshipping at the altar of double blind studies now. But obviously a reasonable person can tell for sure that something is working. In the first place I think we have to take account of this very interesting increased bowel tolerance which, of course, doesn't need a double blind study to prove. It demonstrates to anyone who has ever experienced it that something is going on that they just don't understand. But the result is certainly spectacular. Let's say you're testing a medication and get results that are, say, 40:60. Then you're going to have to double blind it. But if you hook up an IV and run a material in rapidly and within minutes you see that the symptoms of diseases are mitigated then

you really don't need a double blind. It would be very easy to take a hundred patients admitted with hepatitis to a large university center and give them ascorbic acid and compare them with the last hundred hepatitis patients that were admitted to that hospital. I think that the results would be convincing. The problem with double blind tests is that in a way you sometimes deceive yourself.

Q. Yes, I can almost see a group of patients each somehow identified as having a 100-gram cold. We split them. Give one group "C" and try to find something sufficiently sour to pass for vitamin C, which the patient can tolerate at 100 grams per day.

Have you published what you have done in the standard medical journals?

Why in CHEMTECH?

A. No, but I've tried. My manuscripts were rejected.

Q. What did the referees say? In chemical periodicals the editor refers the paper to referees he chooses, experts

in the field, and then forwards their comments, anonymously usually, to the author. Is that the practice in the medical periodicals?

A. In my case the manuscripts were just flat out refused.

Q. Just like that without any explanation?

A. Yes.

Q. Wow. Might it have something to do with an establishment protecting itself or something like that?

A. Well...

Q. Do you want to comment on this?

A. Well, really I don't. You know I really believe that the doctors involved in these decisions don't believe that this is true.

Q. In other words you think they're saying that this qualified physician who has an international reputation for his hip prosthesis has made all this up. Colds, flu, hepatitis, mono ..., diseases a second-year medical student could recognize with high probability ... they don't *believe* this?

A. Yup. They just don't believe it. They think I'm deceiving myself somehow. They see placebo effects as being very significant. I agree that placebo effects are significant, but I don't believe that they are *this* significant. Take the effects on children, on infants. In seven years I've not had to hospitalize a child who came in with a virus-induced fever.

Q. Wouldn't placebo effects be non-quantitative? If the physician gives the patient a couple of pills it won't make any difference whether he gives him big ones or little ones or two instead of four. How can we explain by placebo effect such a thing as a 50-gram cold and a 100-gram cold? It's the bowel telling you which you've got, not your head.

A. No question. This increased bowel tolerance is a spectacular phenomena that I wish all physicians could experience because once they experience it they know that something is going on.

Q. Is it conceivable that one can psychogenically control a case of diarrhea that normally appears at 10 grams and now all of a sudden when you're ill appears at 200 grams?

A. Oh there's no way that this can be psychogenic.

Q. And so we have, we have a problem here ...

A. I think of communication.

Q. How do you feel about it?

A. Well, it worries me. It worries me in a lot of ways.

Q. The normal procedure in chemistry is if peers question a colleague's results, published or otherwise, they endeavor to repeat this work in their own laboratories. If they succeed they publish and if they don't succeed they publish. Doesn't that happen in medicine?

A. Well, understand first that this wasn't even published so people know of it only by word of mouth. One of the three physicians here in town is now using vitamin C for at least hepatitis cases. A fellow physician in Reno he's convinced to use it was amazed at the results. I treated an orthopedic surgeon in Carson City who had a serious case of hepatitis, and another in San Bruno who phoned because he knew of my work. Both these physicians are convinced beyond doubt that my megadose therapy altered the course of their hepatitis. But my work isn't widely known. I'm hoping that our chat will help, but it isn't easy to introduce new methods in medicine. It used to be that if a new physician came to town and he had

some new treatment then the senior physicians in the community would look at him, yes; but, because they had seen so much development in the past, it was a professional thing to stay out of this physician's way unless he showed that he was doing something really wrong. Competition would prove whether or not his ideas were right.

Malpractice!

Q. Patient would tell patient whether they believed this physician cured them or didn't?

A. Right. Now we're all living in a state of anxiety called the Malpractice Crisis. The first physician in town who does something new is not employing "practice of the community," and the last physician in town who adopts some procedure is also not employing "practice of the community." So there's a feeling that if we stop all progress, we will all get so practiced at "practice of the community" that we can't get sued anymore.

Q. "Practice of the community?" That's a legal term?

A. Yes, it's the criterion by which a physician is judged in court. Any change creates a debate within the medical community, which under ordinary circumstances is healthy, but now a change means that the "practice of the community" is in a state of flux so that attorneys for either side can get physicians for their side to testify that the defendant physician was or wasn't using "practice of the community." Take your pick.

Q. Do you have any idea how big a "community" the law uses in defining "practice of the community?"

A. I'm certainly not an expert on that, but as I understand it, it used to be more of a local community. Now it's getting to be more ... almost an international community.

Q. International?

A. Yes, this creates a problem for us in rural medicine because when we're away from the large medical centers we don't have the facilities that they have in the big city. Sometimes we're forced to render care ... don't have time to send them to the city ... yet there can be criticism of the equipment that we have, for instance, and there can be a suit.

Now just because a suit is filed doesn't always mean that it's going to prevail, but defending a suit is a *misérable* experience for the physician. It puts him in a state of anxiety. The more idealistic he is—the more he used to care about patients—the worse it hurts him.

Q. And you've seen intensification in this. Seen it, for example, in what you pay for insurance. How has the premium changed over the years?

A. It went into a mad frenzy right after no-fault automobile insurance went into effect. Attorneys didn't seem to have anything to do so they launched a campaign against physicians. When I started practice I paid about

\$800 a year for insurance. That was in 1969. I quit surgery because of the whole malpractice thing three, four years ago, when the jump was from \$4000 to \$8000. In some cases insurance now costs \$20 000 to \$30 000 for an orthopedic surgeon.

There's an interesting paradox here: the more surgery a person does, the more insignificant a large malpractice premium becomes in his overhead. So a surgeon who tries to avoid doing surgery is the one who's kicked out of the surgical field first. I know a fellow in San Francisco who does, oh maybe 100, 150 laminectomies a year... that's back surgery, disk removal. Anyway, some people do a lot of laminectomies but the frequent need for them is a debatable point in orthopedics. So what happens? Those of us who feel that fewer should be done are in a sense being taken out of competition by the malpractice crisis.

Q. Are you saying that a physician who is doing this kind of surgery is going to pay, say, \$30 000 a year for insurance no matter how many such operations he performs? For our friend who does 150 operations a year—3 a week—that's \$200 per case just for insurance. It's obvious what happens if he talks himself out of doing half of those.

What kind of patient do you most often find involved in malpractice suits?

A. First he's a patient with the more serious kind of problem, so that means that the more specialized a physician is, which means often the more competent he is, the more likely he is to get sued. The neurosurgeon, the cardiovascular surgeon ... they get sued the most because they take on the most responsibility. The orthopedic surgeon gets sued a lot not only because he handles difficult problems, but also because many of his patients have had accidents, so their cases are automatically reviewed by attorneys. It's interesting that the doctor who avoids serious problems is perhaps less of a scientist, less up on his work, concentrates on simple things, has a good personality, relates well with his patients. He's less likely to get sued.

Q. Is he the one who sets the "practice of the community," not deviating not doing anything new?

A. That's right. Whereas the highly skilled person who may be a little introverted ... that's the only reason he can stand to be that skilled ... has to go to class a lot, spend his life studying, not watching football games, drinking beer Saturday night...

Q. Reading a lot of journals?

A. Yeah, so that this fellow may not have the personality but he's the specialist and he's more likely to get sued.

Q. Fair enough. But maybe tonight we can break that lock step. Let me buy you a beer before we call it a night.

A. OK, and I can tell you about the hip prosthesis I developed. I don't have hours *that* early tomorrow ...

EPILOGUE

It's amazing, sometimes, to what extent an Editor will go to assure the quality of his publication! Like in this case—I went out and caught the flu. Wednesday evening I realized my scratchy throat had gotten worse and I ached, so after dinner, I added two more grams of ascorbic acid to the four I'd already taken that day. By 10 my fever was a bit over 101° so I took another 3 grams, which seemed like a lot, and went to bed. I probably should have continued popping pills all night 'cause next day I woke up achy with my temperature already a degree above normal. I im-

mediately started a vitamin C regime of 4 g per hour; by 11 my temperature was down and I felt fine. That afternoon, with my pocket full of gram-size pills I attended a Board meeting, an open house (SIPI), a dinner of the Research Directors Association, walked briskly about 2 miles to and from the train and tumbled into bed, tired but symptomless. I'd kept up a steady 2 g/h all afternoon so my daily take was 44 g.

That night I didn't sleep very well: I must have groped to the John a half dozen times. (Dr. Cathcart did warn me

of that. Said he, "I even got blamed for an apparent increase in Incline Village's population. " "Oh, does C do *that*, too?" "No, but they use a T.V. toilet-flush index to estimate population and in the flu season in Incline Village it goes up."

On my 2:00 a.m. return trip I started medication so that by wake-up at 7:30 I had 15 g in me already ... and a low fever. I upped the dose to 5 g/h and then at noon to 6 g/h. That's equivalent to 144 g/24 h day. That calculation convinced me that I must be really sick, though I felt fine—well, not absolutely. I had finally gotten close

enough to bowel tolerance to have developed a fine case of *magensprache* (literally, stomach speaking); and was so flatulent I felt like the Hindenberg reincarnated. Anyway, having convinced myself that I was really ill, I phoned Dr. Cathcart.

"Yes, at that dosage you're close to something that would put you in the hospital if you weren't on ascorbic acid at bowel tolerance."

"Yes, take it every hour; No, a 6 g dose isn't too much. My experience is more with powder than pills but I've used a single dose of 2 tablespoons of powder in water for mono." (That's about 25 grams)

"You could use a controlled release formulation at night."

"Oh, I'd *certainly* see your physician. You could have something bacterial on top of the virus. He may want to do a culture. *Do* see him."

"Yes, you *are* contagious but at least you're not sneezing all over everyone."

So, off I went to my internist and tried to explain to him why I was there without any symptoms.

"Oh, you have something; throat's red. No need to culture it now. Just take it easy for 5 days. If you want to take all that vitamin C, go ahead. It'll just come out in your kidney; probably can't do any harm. Just don't get a lab test for gout. I've seen a lot of false uric acid positives since Pauling started everyone on ascorbic acid."

"But couldn't I have something terrible that the C is masking? It takes all the symptoms away."

"I can do that with aspirin. Call me if anything comes up. You're vulnerable even if you feel good."

Saturday, day three, I took it easy. Also I took about 75 g of C. I didn't keep track. By then I was popping 1000 mg pills like bar peanuts.

Sunday I spent in the office. At 30 g in four hours I found out what happens if you exceed bowel tolerance. No big deal. The rest of the day I felt fine and took no more pills 'til it was time for dinner and the theater. Then I popped a 5 g "prophylaxis".

Monday, day five, I decided to see if I was well: I took "only" 4 g and waited to stop aching and sneezing. By noon I was functional but mildly miserable so I tried my physician's aspirin routine. It didn't help much. But a 5 g dose of C at 3:00 p.m. and another at 4:00 had me feeling fine—just a bit gassy.

By Thursday, day eight, I had morning catarrh, more severe than usual, a throat tickle that came and went, and four empty, 100 g, vitamin C bottles.

Friday found me fine on 4 g maintenance.

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Write On

continued from page 259

RE: SYMPTOMECTOMY with vitamin C:
March 1978 CHEMTECH: This surely is a classic article which should be widely circulated as it is at once an essay and a satire on the scientific establishment and the self-aggrandizement business which has come to be a major characteristic of modern science. As science itself, this article is a double-edged sword, for it both slashes enemies and cuts friends. On the one hand, it feeds the "anti-scientific" fires, which have been burning brightly lately, and is bound to be widely quoted by many health faddists as evidence that the scientific establishment is not really relevant. "The tragedy of modern science is that it is only certain about things which are absolutely trivial" (direct quote of lay letter to editor).

The quotes of the (late) Sherry Lewin, as an authority on vitamin C mechanisms of action, are inappropriate. Dr. Lewin (who was a close friend) was an imaginative, enthusiastic physical chemist in my opinion who had to write books to get many of his ideas published. I found his ideas new and exciting—well worth pondering—but did not necessarily feel I had to believe all of them. I do not think that he thought all his ideas were proven either.

This article is an indictment of the "Scientific Establishment" who would not publish Cathcart's ideas where they could be discussed and confirmed or denied. Again, are the editors of scientific and medical journals only sure about things that are absolutely trivial? ... While one is wary of the small town MD making 'a priori' conclusions without conventional experimental evidence, where would he go for funds to try to test his ideas experimentally? ... Would the Peer-Review-Grant system give him support, or would they reject him, saying that he is "not-qualified" to do biochemical and metabolic research? ... Has our scientific establishment assumed such a defensive position that we are no longer willing to listen to imaginative new ideas from people like Lewin and Cathcart? ... Are we really so confident of our scientific precepts and logic that we can reject such ideas out of hand?

Perhaps the recent CHEMTECH article by Paul Mok (Dec. 1977, p 20) puts things in perspective. He would likely classify people like Lewin and Cathcart as "Intuitive Personalities" most interested in ideas and concepts. This might be contrasted to the "Thinker" type of scientist who is most interested in "Facts" and "Logic"—the bricklayer type building up the edifice of science by accumulating data and publishing 40-page papers on data alone. Perhaps the balance between the "intuitives" and the "thinkers" has been lost. Perhaps the Peer Review System and the system of choosing editors of "reputable" journals favors the "thinkers" over the "intuitives"? Have the "thinkers" really come into control of the scientific administration process? Wouldn't it be too bad if people like Paul St. Gyorgi, Linus Pauling, Sherry Lewin, and Robert Cathcart continue to be kept out of the smoke-filled rooms where decisions are made on scientific priorities for funding and publication on critical issues of the day? ...

Thomas R. Henderson
Albuquerque, N.Mex.

P.S. I wonder if I shouldn't submit all my future manuscripts to CHEMTECH first. Those which you reject because they are non-controversial, unimaginative and trivial would then be readily published in almost any other journal I would select...

I have read the article, 'Symptomectomy' in the February CHEMTECH. Devotion of space to such anecdotal material is, to me, a serious error in editorial judgment. Indeed, the desirability of publishing even good clinical material in CHEMTECH is lost on me.

The personal epilogue to the article is tasteless in content and, in publication, another lapse in editorial judgment.

Is CHEMTECH changing its policies as to what is suitable material?

Jack P. English
Grantham, N.H.

it yourself you surely know what I mean.

Depending on where you buy it, those 250-gram bottles can run as high as \$16. For a working person this beats a day or two in the hospital, but pity the poor college student (and quite a few will read your article) who has to count the nickels and dimes. Johnny, don't throw the aspirin bottle out yet!

How about another article on how to synthesize vitamin C in the kitchen from some cheap starting material, say brown sugar!

J. Bates
Hixson, Tenn.

In reading the interview with Dr. Cathcart (CHEMTECH, Feb. 1978, p 76) I began to wonder if it was really the vitamin C that was producing the reported beneficial effects. Perhaps, these effects could have been produced by some impurity or *byproduct* of vitamin C decomposition which may be present only in extremely small amounts, but which would show up with the massive (!) doses used.

E. D. Miller
Nanticoke, Pa.

Regarding your article "Symptomectomy" about Dr. Cathcart's use of vitamin C: *How can you print such dangerous garbage?*

Robert E. Pincus, President
Permier Malt Products
Milwaukee, Wis.

In your otherwise superb article on vitamin C therapy (CHEMTECH, Feb. 1978, p 76) why didn't you say a few words about the cost of such treatment? Having tried

Write On

continued from page 519

Reader Robert Pincus, who called the Cathcart Vitamin C Symptomectomy article "dangerous garbage (June CHEMTECH), should be encouraged to publish the results of *his* research, which proves that it is!

"Poor" students and others can buy vitamin C from drug supply houses for \$9.50/kg. Bronson Pharmaceuticals, La Canada, Calif. 91011 is an example of such a supplier.

Gregor H. Riesser
Houston, Tex.

I enjoyed reading Luberoff's article on "Symptomectomy" in the February CHEMTECH, but enjoyed even more reading the letters attacking the article and its conclusions (re: J. P. English and R. E. Pincus, CHEMTECH, June 1978).

The attackers write about "dangerous garbage" and/or merely "anecdotal material" without further comment. The term "anecdotal material" is used to dismiss findings of other physicians who have experimented with the use of vitamin C and other drugs in the treatment of numerous disorders. What I do *not* see in attacks such as these are references to materials which explain some of the admittedly interesting observations reported by scientifically-trained medical practitioners. All the more confusing when one considers:

(i) that great advances in the field of medicine have resulted from such "anecdotal" observations by individual scientists who have dared to consider unorthodox but reasonable explanations for specific diseases and/or disorders. In fact, I challenge your readership to provide references describing major advances in medicine which have been made as a result of "rigorous clinical testing"—including, of course, all of the latest "accepted" techniques (double blinds, control groups, placebos, and the rest).

(ii) that the detailed observations of physicians such as Cathcart adjure rational, scientific explanation. Why, for example, does the body exhibit an increased tolerance for vitamin C when the symptoms of a cold are present? Until questions such as these have been answered by the "responsible" medical opinion-makers, Cathcart's hypotheses are certainly as acceptable as anyone else's until they are rationally and scientifically disproven.

R. C. Forrester III
Knoxville, Tenn.

p.s.

Ever since we wrote about the mega mega dose, "bowel tolerance titration" with Vitamin C (CHEMTECH, February 1978), we've been hearing anecdotal cases pro and con. Now L. K. Altman, writing in the *New York Times* of September 27, tells of a trial mega dose of Vitamin C that was put through at the Mayo Clinic. The malady was cancer and the dose was 10 g of C per day. The result was no discernable effect—63% of the test group reported feeling better vs 58% of the control. The median survival rate of both groups was "about seven weeks".

One wonders what 10 g/d was supposed to do for patients who were that "terminal" when a garden variety cold can "consume" 50 g/d, flu or mononucleosis over 100 g/d and some severe viral infections over 200 g/d?

The Mayo group, headed by E. T. Creagan, undertook this more positive study because earlier Scottish studies, in which Linus Pauling collaborated, didn't randomize their sample "scientifically".

Checklist

Corporate myths	71 ☐	The ruts we're in often stem from no more logic than some aboriginal taboos, says Pacifico ; but digging out can cost you your head.
Quads on campus	73 ☐	Ethics, recently strengthened by law, will bring more handicapped people into the work place. Thus Lipps' rare insight into how the most severely handicapped cope in college is prelude.
Symptomectomy with vitamin C. A chat with Robert Cathcart, M.D.	76 ☐	"I still get colds but now I know what to do about them" (and a lot of other diseases), says Cathcart in this interview that also probes problems of today's medical practitioner.
Condensation product and method of making same	88 ☐	This month's exemplary patent is the one that just got Leo Baekeland elected to the National (U.S.) Inventors Hall of Fame.
How to read a patent	91 ☐	If reading our first couple of Landmark Patents has you wondering how best to use patents, Maynard's new book, from which this article is condensed, is the best place to start.

Effect of Micronutrients on Morbidity and Duration of Hospital Stay in Childhood Pneumonia

*Wahed MA¹, Islam MA², Khondakar P³, Haque MA⁴

A cross-sectional and controlled clinical trial was conducted in under-5 children to compare the effects of supplementation of five micronutrients (vitamin-A, vitamin C, vitamin E, folic acid and zinc) on the morbidity and on the duration of hospital stay in pneumonia. Data were collected from 1150 children. Among them 350 children were excluded for various reasons and finally data from 800 children were analyzed. Among these 800 children 59.00% (475) were male and 41.00% (325) were female. The mean±SD age was 6.5±5.6 months and 56.25% (450) were infants. The children were divided into two groups-400 in control group and 400 in intervention (case) group. In both the groups, specific treatment was given by ampicillin and gentamycin. In intervention group, five micronutrients were given in 200 children from the day of admission and continued up to discharge. Another 200 children were again divided into 5 sub-groups (40 in each sub-group) and a single micronutrient was given in the same way in each sub-groups. All the subjects were suffering clinically from severe pneumonia and radiologically from bronchopneumonia. Cases and controls were matched by parents' occupation, education level, economic status and family members. All the children were fully vaccinated as per existing EPI schedule of the country, partially breastfed up to six months and after six months weaned by carbohydrate rich diet. All the children were in mild (grade I) PEM according to Gomez's classification. Venous blood was collected for estimation of serum level of five micronutrients from all the samples before starting treatment by standard procedures. The average blood level of all the micronutrients was low. The average duration of hospital staying was 6.75 days in intervention group and 7.75 days in control group ($p<0.01$). Chest indrawing and fast breathing disappeared earlier in the intervention group ($p<0.01$) suggesting that supplementation of micronutrients decrease the morbidity and duration of hospital stay of children suffering from pneumonia.

[Mymensingh Med J 2008 Jul; 17 (2 Suppl): S77-83]

Key words: Pneumonia, Micronutrient supplementation, Morbidity

Introduction

Acute Respiratory Infection (ARI) is the most common cause of morbidity of under-five children in Bangladesh and a great public health concern^{1,2}. Among all the ARI's, pneumonia occupies special attention because of a significant proportion of childhood mortality occurring due to this ailment^{3,4}. On average, children have 4-6 ARI episodes each year; 5-8 episodes per child per year in urban areas and 3-5 in rural areas^{4,6}. One third of all admissions in hospitals of children are sufferers from ARI and there are 85,000 deaths due to pneumonia each year in Bangladesh^{7,9}.

On the other hand, many children suffer from deficiency of micronutrients and more than 2 billion children are sick or disabled as a result of micronutrient deficiency in the world and a major portion are in the South-East Asia including Bangladesh¹⁰. Vitamin A deficiency causes

epithelial defects, impairs the immune system and reduces children's resistance to diarrhoea, measles and increases the incidence and severity of pneumonia^{11,12}.

1. *Dr MA Wahed, Associate Professor, Department of Paediatrics, Rangpur Medical College, Rangpur, Bangladesh; E-mail: mawahed@mail.mayaonline.net.bd

2. Professor Md Anwar Ul Islam, Professor of Pharmacy, University of Rajshahi, Rajshahi, Bangladesh

3. Mrs Proma Khondakar, Associate Professor, Department of Pharmacy, University of Rajshahi, Rajshahi, Bangladesh

4. Dr Md Azizul Haque, Associate Professor, Department of Paediatrics, Mymensingh Medical College, Mymensingh

*for correspondence

Zinc acts as an immunomodulant and its deficiency is associated with increased prevalence and delayed recovery from pneumonia. In a trial in our country on children aged 6-12 months of age, simultaneous weekly administration of zinc and iron was associated with 40% lower risk of severe pneumonia^{13,14}. Supplementation of zinc has also been found to reduce risk of pneumonia by 45% and duration of hospital staying by 41%¹⁵⁻¹⁷. Folic acid, Vitamin C and Vitamin E play roles as antioxidant and decrease the severity of pneumonia by protecting the damage of cells and tissues from oxidants. A study conducted on infants and young children with vitamin C at a dose of 500mg IM six to twelve hours interval showed that 3-7 injections gave complete clinical and x-ray response in case of virus pneumonia¹⁸.

So, it is obvious that there is relationship between incidence and severity of pneumonia and micronutrient deficiency. Moreover, micronutrient deficient children require more admission in the hospital and more costly drugs are needed and they also require longer time in hospital^{5,7,8}. This causes loss of resources from the parents because Government Hospitals usually run short of costly drugs and maximum numbers of these drugs are usually bought by the parents from outside shops¹⁹. In Bangladesh, only few studies were conducted to assess the micronutrient supplementation on morbidity of pneumonia in under-five children. For this reason, the study was conducted to compare the effects of supplementation of micronutrients on the severity of pneumonia and duration of hospital stay.

Methods

The study was a cross-sectional, prospective and controlled micronutrient supplementation trial. The study was conducted in the Paediatrics Department of Rangpur Medical College Hospital for a period of three years from 1st July 2004 to 30th June 2007. All the children admitted with various types of pneumonia were the study population and among these, children having the clinical diagnosis of severe pneumonia and radiological diagnosis of bronchopneumonia on admission were selected as samples. The statistical formula $4\sigma^2/L^2$ was applied to determine the number of samples. Here σ was the standard deviation of average stay in hospital, ± 4.8 in this study and L was acceptable variation,

0.5 day in this study at 95 % confidence interval^{20,21,22}. In this way, the optimum number of samples became 384. This was rounded to 400 and then doubled ($400 \times 2 = 800$) since there were two independent groups. The sampling method was systematic sampling and every 1st patient was given the intervention and 2nd patient was treated as control from a prepared register.

A standard questionnaire was developed in accordance with the study objectives to obtain relevant information. The questionnaire contained some independent variables such as age, educational status of the parents, monthly family income of the parents, breast feeding pattern, time and type of weaning foods, immunization status, vitamin A supplementation, vitamin C supplementation, vitamin E supplementation, supplementation of folic acid, supplementation of zinc and weight of the child. The dependent (outcome) variables were morbidity from pneumonia and duration of hospital stay in days. Few months before starting the formal study, the questionnaire was pre-tested among children of the ward. During pre-testing, all the variables were considered except collection of the blood. Then it was modified as required and finalized for collection of data. The Questionnaire was in English language.

History of illness of the child was collected from the mother or guardian who attended the child in hospital. Clinical examination was carried out on the child on the day of admission and everyday up to discharge. The 'Bar Scale' designed by National Nutritional Council of Bangladesh was used to record the body weight. All the questionnaires were filled by the investigator himself. The children who left the hospital on 'risk bond' or 'absconded' from the ward or 'expired' during treatment were excluded from the analysis. Also those who developed a complication of pneumonia, were suffering from other severe systemic diseases with pneumonia, required antibiotics other than the ampicillin and gentamycin and whose parents did not give consent for drawing blood were also excluded from the study. The children who were in a convalescent stage from another disease and were taking or took any of the micronutrients within last one week also excluded. Initially data were collected from 1150 children and after exclusion only 800 children were selected for analysis.

Answers of the mothers and findings of clinical examinations were recorded in the "Interview Schedule". The nutritional status was assessed according to Gomez' classification. In all children, venous blood was taken before starting treatment. Then the blood was sent to the laboratory for centrifugation and separation of serum for estimation of serum level of micronutrients. The method of analysis was High Performance Liquid Chromatography (HPLC)²³⁻²⁸ for vitamin A, vitamin C, Vitamin E, colorimetric method for zinc^{29,30} and ELISA³¹ for folic acid. The selected laboratories were Padma Diagnostic Center, Dhaka and Apollo Diagnostic Center, Rangpur. Tests were performed by the consultants experienced in the respective fields.

The children were followed daily up to discharge from the hospital. The criteria of discharge were free from the clinical features of severe pneumonia for two consecutive days. There were six groups of children- one was intervention group (N=400) and the other control group (N=400). Again the intervention group was broken into six groups (200 + 40 + 40 + 40 + 40 + 40). In intervention group, specific treatment was given by Ampicillin (50-100 mg/kg/day) and Gentamycin (5-7mg/kg/day) in injection for six days along with micronutrients in adequate doses. The brands of micronutrients were products of reputed Pharmaceutical companies. In 200 children, all the 5 micronutrients were given along with specific treatment but only one micronutrient was prescribed in each of 5 sub-groups (40 in each sub-group). In control group, only specific treatment was given without micronutrients. Compliance was checked by Assistant Registrar every day during ward rounds. The drugs were administered by mothers and nurses. Verbal or written consent was taken from the parents maintaining the principles of Helsinki Declaration^{32,33}.

After completion of collection of data, all filled up 'Interview Schedules' were checked for missing values and outliers. The data were then entered into a computer. The analysis was performed by SPSS+PC programme according to objectives. Descriptive statistical tests were applied to age, monthly income and biochemical variables. Univariate, multivariate and ANOVA were also performed as necessary.

Results

Among 800 children studied 56.25%(450) were infants, 23.75%(190) were within 1-2 years, 11.25%(90) were within 2-3 years age group, 6.25% (50) were 3-4 years age group and 2.50% (20) were 4-5 years age group. Infants suffered more from pneumonias. Of the study population 59.00% (475) was male and 41.00% (325) was female. The mean± SD age was 6.5±5.6 months (Table I). The average serum level of different micronutrients were vitamin A (retinol) 0.60 µmol/l, vitamin C (ascorbic acid) 32.50 µmol/l, vitamin E 6.50 µmol/l, folic acid 3.50 nmol/l and zinc 9.70 µmol/l. The average serum level of all the micronutrients considered was lower than the normal level (Table II).

Table I: Distribution of children according to age and sex (N=800)

Age group	Sex of the children		Total (%)
	Male (%)	Female (%)	
Birth-1 year	255 (31.88)	195 (24.37)	450 (56.25)
1-3 year	170 (21.24)	110 (13.74)	180 (35.00)
3-5 year	50 (6.25)	20 (2.51)	70 (8.75)
Total	475 (59.00)	325 (41.00)	800 (100.00)

Mean age± SD = 6.5 ± 5.6 months

Table II: Average baseline serum concentrations of micronutrients in the samples (n=800)

Item	Average (serum) level ± SD	Normal value
Vitamin A	0.60 ± 0.05 µmol/l	00.70-1.50 µmol/l
Vitamin C	32.50 ± 0.15 µmol/l	34.00-113.00 µmol/l
Vitamin E	6.50 ± 0.45 µmol/l	7.00-21.00 µmol/l
Folic acid	3.50 ± 0.04 nmol/l	4.10-20.40 nmol/l
Zinc	9.70 ± 0.74 µmol/l	09.8-18.1 µmol/l

ANOVA p<0.10 (Poorly significant)

The average duration of hospital stay of children in control group was 7.75 days and in intervention group was 6.75 days. The average difference was 12.90% (p<0.01) in the groups (Table III). The

infants in both the groups took more time in hospital than the older children. The duration of hospital stay of children who got all the 5 micronutrients, vitamin A and zinc was shorter than those children who got vitamin C, vitamin E and folic acid (Table IV). There was no difference in time of disappearance of fever and feeding difficulty. But fast breathing and chest indrawing disappeared earlier ($p < 0.01$) in micronutrient group than control group (Table V).

Table III: Duration of hospital stay of control and intervention group (N=800)

Age group	Duration (Days)			
	Control group		Intervention group	
	No.	Duration	No.	Duration
Birth-1 year	229	7.78	221	7.23
1-3 years	136	7.75	144	6.75
3-5 years	35	7.75	35	6.50
Total	400	7.75	400	6.75

$p < 0.01$

Table IV: Duration of hospital stay of intervention group (N=400)

Number	Average duration (Days)
Who got 5 micronutrients (200)	6.05
Who got vitamin A (40)	6.50
Who got vitamin C (40)	7.00
Who got vitamin E (40)	7.00
Who got folic acid (40)	7.00
Who got zinc (40)	6.75

$p < 0.05$

Table V: Effect of micronutrients on selected clinical signs

Signs	Duration of disappearance	
	Control group (Days)	Micronutrient group (Days)
Fever	2.0	2.0
Feeding difficulty	2.0	2.0
Fast breathing	4.5	4.0
Chest indrawing	3.5	3.0

$p < 0.01$

Discussion

Among the children studied, 59.00% (475) were male and 41.0% (325) were female. The male female ratio was 1.4:1. A study conducted on children suffering from pneumonia in Dhaka Shishu Hospital showed male and female ratio as 2:1³⁴. Two other studies^{35,36} conducted abroad showed male and female ratio as 61:39 and 69:31 respectively in hospitalized children suffering from pneumonia. This may be due to the fact that male children in our society are given more care than female ones due to various reasons or male children actually suffer more from diseases than female ones³⁷. The study shows that 56.25% (450) children were infants and the Mean $\pm$ SD age was 6.5 $\pm$ 5.6 months. One study conducted in our country has shown that ARI most commonly (84%) occurs in infancy followed by 1-4 years of age, which is consistent with the present study³⁸. The individual values of the levels of micronutrients in the samples were either marginally normal or below the normal level. WHO estimates that about 2.70% pregnant women suffer from frank vitamin A deficiency with a vast number suffering from borderline deficiency in developing countries³⁹. As a result, the fetuses get less nutrients in utero and are born with deficit of micronutrients. The rate of exclusive breast feeding was also low in the samples which resulted in getting less micronutrients. The non-breastfed children were also not properly weaned. Those weaned, the foods contained low amount of micronutrients. This may be also the cause of micronutrient deficiency⁴⁰. Widespread micronutrient deficiency in preschool children and mothers has also been demonstrated in Nigeria where 40.00% of the boys had vitamin A deficiency and 47.00% had vitamin C deficiency⁴¹. In Nepal, there is widespread multiple micronutrient deficiency in pregnant women and 12.00-18.00% of the mothers suffer from night blindness during pregnancy^{42,43}. The average duration of hospital stay of children in control group was 7.75 days and that of children in intervention group was 6.75 days. One study conducted in Brazil on children aged 6 months to 4 years has shown the duration of an episode in hospital as 6 days which is almost similar to the duration of this study⁴⁴. Another case-control study in Brazil on efficacy of vitamin A treatment in non-

measles pneumonia has shown the average duration of an episode as 7.60 days in cases and 7.50 days⁴⁵. Although the difference of one day may be very short but it is significant in the sense that discharge of a patient one day before the expected period saves resources of the hospital. Micronutrients enhance immune status and prevent tissue damage by antioxidant activity. They also exert enhanced regeneration of epithelium. As a result, morbidity is reduced and there is early recovery from the disease⁴⁶.

The duration of hospital stay of children who got all the 5 micronutrients was shorter than those children who got one micronutrient. As most of the children studied were malnourished and there were deficiencies of multiple micronutrients in these children, their immune status was probably very low. So, the children who got all the micronutrients, their immune status were probably improved to enhance the cure of the diseases than the children who got a single micronutrient. One study in Vietnam on 163 children of aged 6-24 months there was simultaneous low concentration of several micronutrients (haemoglobin, retinol and zinc) and after supplementation of micronutrients in these subjects, their micronutrient status were improved and took less time to be cured from acute infection which goes in favour of this study⁴⁷. One review study has also described that micronutrient such as vitamin A and zinc given as a therapy may benefit the clinical course of childhood pneumonia⁴⁸. Another study in Indonesia has shown that micronutrient supplementation in children improves the micronutrient status⁴⁹.

There was no difference in the mean number of days of disappearance of fever and feeding difficulty. But fast breathing and chest indrawing disappeared a bit earlier in intervention group. One study in Tanzania has shown that the average duration of hospital stay was 4.2 days and there was no difference of disappearance in the mean duration of fever in children suffering from pneumonia⁵⁰.

Conclusion

Every study has some weaknesses and constraints. Micronutrient levels were done only before starting of treatment. They were not done at the end of the treatment due to economic constraints, which could be helpful to see the difference between the serum

levels of micronutrients. Vacutainer test tubes were not used to draw blood which is ideal to prevent the contamination with air. Blinding of the samples has not been done which could increase the quality of the study. If tissue levels of micronutrients could be done, it could reflect the actual micronutrient status in the samples. In spite of these constraints, the results reveals that micronutrient deficiency is abundant among children of Bangladesh especially among under-five children in the northern zone of country and micronutrient supplementation may be beneficial as an adjunct to specific antimicrobial therapy among hospitalized children suffering from pneumonia.

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Journal of Applied Nutrition Vol. 23, No's 3 & 4, Winter 1971

Observations On the Dose and Administration of Ascorbic Acid When Employed Beyond the Range Of A Vitamin In Human Pathology

Frederick R. Klenner, M.D., F.C.C.P. (1907-1984)

Comment by R.F. Cathcart:

The original of this paper repeatedly refers to intravenous *ascorbic acid*. From talking with Klenner, from talking with his wife, Annie Klenner, who served as his nurse, and from my personal experience, it is clear that he meant *sodium ascorbate*. [See my article on how to make intravenous C solutions](#). I am especially indebted to Annie Klenner for her descriptions of how Fred made the intravenous solutions of sodium ascorbate.

Editor's note:

In light of the above, for clarity I have changed all 201 occurrences of "ascorbic acid" in the text to read "ascorbate". (Ascorbic acid is also known as hydrogen ascorbate.)

Apparently Cathcart had lifted his copy from [this version on AscorbateWeb](#). I worked on that for Bob then cloned the version on Bob's site to this page and did some more work on it. The AscorbateWeb copy has also had more work done on it.

—Dave Yost 2002-11-29, 2014-05-28

[International College of Applied Nutrition] Editor's Note:

Because of the unusually high amounts of ascorbate used in Dr. Klenner's treatment as reported in his paper, we asked him to verify amounts mentioned. Following is his answer:

To the Editor of the ICAN Journal:

This will confirm that all 'quantity' factors given in my paper are correct and can be confirmed from

hospital and medical office records. The notation relative to 150 grams represents the amount used for reversing pathology in a given case and was the amount given over a period of 24 hours. (The I.V. was continuous.) This was given in three bottles of 5D water, decanting only enough from 1000 c.c. to be replaced by the 'C' ampoules.

Recently the FDA has published a 'warning' that too much soda-ascorbate might be harmful, referring to the sodium ion. In reply to this I can state that for many years I have taken 10 to 20 grams of sodium ascorbate by mouth daily, and my blood sodium remains normal. These levels are checked by an approved laboratory. 20 grams each day and my urine remains at or just above pH 6.

Signed:

Fred R. Klenner, M.D.

Sections below:

[Body of paper](#)

[Summary](#)

[Appendix](#) - more case histories

[Bibliography](#)

[Klenner Biography](#)

Journal of Applied Nutrition Vol. 23, No's 3 & 4, Winter 1971

**Observations On the Dose and Administration of
Ascorbic Acid
When Employed Beyond the Range Of A Vitamin
In Human Pathology**

Frederick R. Klenner, M.D., F.C.C.P. [1907-1984]

Ancient History and Homespun Vitamin C Therapies

Folklore of past civilizations report that for every disease afflicting man there is an herb or its equivalent



that will effect a cure. In Puerto Rico the story has long been told “that to have the health tree **Acerola** in one’s back yard would keep colds out of the front door.”[1] The ascorbate content of this cherry-like fruit is thirty times that found in oranges. In Pennsylvania, U.S.A., it was, and for many still is, **Boneset**, scientifically called **Eupatorium perfoliatum**[2]. Although it is now rarely prescribed by physicians, Boneset was the most commonly used medicinal plant of eastern United States. Most farmsteads had a bundle of dried Boneset in the attic or woodshed from which a most bitter tea would be meted out to the unfortunate victim of a cold or fever. Having lived in that section of the country we qualified many times for this particular drink. The **Flu of 1918** stands out very forcefully in that the Klenners survived when scores about us were dying. Although bitter it was curative and most of the time the cure was overnight. Several years ago my curiosity led me to assay this “herbal medicine” and to my surprise and delight I found

that we had been taking from ten to thirty grams of natural vitamin C at one time. Even then it was given by body weight. Children one cupful; adults two to three cupfuls. Cups those days held eight ounces.

Twentieth century man seemingly forgets that his ancestors made crude drugs from various plants and roots, and that these decoctions, infusions, juices, powders, pills and ointments served his purpose. Elegant pharmacy has only made the forms and shapes more acceptable.

Early specifications, action and dosages for administrations

To understand the chemical behavior of ascorbate in human pathology, one must go beyond its present academic status either as a factor essential for life or as a substance necessary to prevent scurvy. This knowledge is elementary. Listen to what appeared in Food and Life Yearbook 1939, U.S. Department of Agriculture[3]: “In fact even when there is not a single outward symptom of trouble, a person may be in a state of vitamin C deficiency more dangerous than **scurvy** itself. When such a condition is not detected, and continues uncorrected, the teeth and bones will be damaged, and what may be even more serious, the blood stream is weakened to the point where it can no longer resist or fight infections not so easily cured as scurvy.” It is true that without these infinitesimal amounts myriads of body processes would deteriorate and even come to a fatal halt.

Ascorbate has many important functions. It is a powerful **oxidizer** and when given in massive amounts; that is, 50 grams to 150 grams, **intravenously**, for certain pathological conditions, and “run in” as fast as 20 Gauge needle will allow, it acts as a “Flash Oxidizer,”[4] often correcting the pathology within minutes. Ascorbate is also a powerful **reducing agent**. Its neutralizing action on certain **toxins, exotoxins, virus infections, endotoxins and histamine** is in direct proportion to the amount of the lethal factor involved and the amount of ascorbate given. At times it is necessary to use ascorbate **intramuscularly**. It should always be used **orally**, when possible, along with the needle.

Scurvy historically the target; today’s goal of high blood levels to cope with self-induced abuses and physiological traumas

If one is to employ ascorbate intelligently, some index for requirements must be realized. Unfortunately there exists today a sort of “brand” called “**minimum daily requirements**.” This illegitimate “child” has been co-fathered by the **National Academy of Science** and The **National Research Council** and represents a tragic error in judgment. There are many factors which increase the demand by the body for ascorbate, and unless these are appreciated, at least by physicians, there can be no real progress. It is vitally important that cognizance be taken of the demand by the body for ascorbate far beyond so-called scorbutic levels. Briefly these demands can be summarized:

1. The age of the individual;
2. Habits — such as smoking, the use of alcohol, playing habits;
3. Sleep, especially when induced artificially;
4. Trauma — trauma caused by a pathogen, the trauma of work, the trauma of surgery, the trauma to the body produced accidentally or intentionally;
5. Kidney threshold;
6. Environment;
7. Physiological stress;
8. Season of the year;
9. Loss in the stool;
10. Variations in individual absorption;
11. Variations in “binders” in commercial tablets;
12. Body chemistry;
13. Drugs;
14. Pesticides;
15. Body weight;
16. Inadequate storage.

Flexible dosage standards explained as minimal standards

With such knowledge it is no longer possible to accept a set numerical unit in terms of **minimal daily requirements**. This is true because of the simple fact that people are different and these same people experience different situations at various times. With ascorbate, today's adequate supply means little or nothing in terms of the needs for tomorrow. Let us start thinking in terms of **maximum requirements**. For too long a time we have under supplied our children and ourselves by accepting through negative ignorance and acquiescence so-called standards. Based on scant data on **mammalian synthesis**, available for the rat, a 70-Kg. individual would produce 1.8 grams[5] to 4.0 grams[6] of ascorbate per day in the unstressed condition. **Under stress**, up to 15.2 grams.[7] Compare this to the 70 mg recommended for daily requirements without stress and 200 mg for the simple stress of the obstetrical patient, and you will recognize the disparity and understand why we have been waging a one man war against the establishment in Washington for 23 years.

Ascorbate not synthesized by man

Work on mammalian biosynthesis of ascorbate indicates that the vitamin C story as is generally accepted represents an oversimplification of available evidence.[8,9,10] This often leads to misinterpretations and false impressions. It has been proposed that the biochemical lesion which produces the human need for exogenous sources of ascorbate, is the absence of the active enzyme, l-gulonolactone oxidase from the human liver[11]. A **defect or loss of the gene** controlling the synthesis of this enzyme in man, blocks the final phase in the series for converting glucose to ascorbate. Virus can mutate cells, X-Rays can do it and it can occur by chance. Such a mutation could have happened, denying all progenies of this mutated animal the ability to produce ascorbate. Survival demanded ascorbate from an exogenous source. This is not remarkable. Other recognized genetic diseases in which a missing enzyme causes a pathological syndrome, in man, are phenylketonuria, galactosemia and alkaptonuria.

It is worthy to note that Sealock and Goodland have ascribed to ascorbate the faculty of being the necessary co-enzyme in the metabolic oxidation of **tyrosine**. The velocity of the oxidation in this reaction is dependent upon the concentration of vitamin C. Tyrosine is essential in breaking down protein to usable amino acid. The scorbutic **guinea-pig's** liver is unable to oxidize tyrosine except in the presence of ascorbate. This suggests a lead in the study of the metabolic abnormality **Alkaptonuria** in humans. Ascorbate administration will correct the alkaptonuria of the scorbutic guinea pig. Its effect on human alkaptonuria has been inconsistent. The reason: Inadequate use of ascorbate.

Biochemist Irwin Stones' concept has practical value

The inability of man to manufacture his own ascorbate, due to genetic fault, has been called “**hypoascorbemia**” by Irwin Stone.[12] This is another reason for abolishing the present concept of daily minimal requirements. The physiological requirements in man are no different from other mammals capable of carrying out this synthesis.

Various procedures testing for the vitamin C levels and Requirements of the body

Various tests have been employed to determine the degree of body saturation of vitamin C, but for the most part they have been misleading. **Blood and urine samples** analyzed with 2:6 dichlorophenol indophenol will give values roughly 7 percent less than when testing with dinitrophenol hydrazine. Gothlin advocates the **capillary fragility test** which is similar to the **tourniquet test** of Hess in results. Both can be used to estimate the quantity of vitamin C necessary to maintain **capillary integrity**. The **intradermal test** of Rotter as modified by Slobody[13] is again gaining new recruits. In principle it is the same as the **lingual test** of Ringdorf and Cheraskin[14] since both are based on the time required to decolorize dye. The lingual test is rapid and simple to perform but it requires a syringe with a 25 gauge needle and a stop watch. Since the dye methods depend on the reduction of the reagent by vitamin C, any substance having a reducing potential lower than the dye is a possible source of interference. Twenty years ago we elected to measure, as a therapeutic gauge, the amount of vitamin C in urine by borrowing on its ability to reduce qualitative Benedict's solution. A 2 plus Benedict's reaction in a known dextrose free urine was accepted as a standard. This test was helpful in gauging requirements for simple stress, but not accurate enough when using needle therapy. Fifteen years ago we developed the **Silver Nitrate-Urine test**[15]. This test employs 10 drops of 5 percent silver nitrate and 10 drops urine which is placed in a Wasserman tube. When read in two minutes it will give a color pattern showing white, beige, smoke gray or charcoal or various combinations of any two depending upon the degree of saturation. We have found this color index test is all one will need for establishing the **correct amount of ascorbate to use** by mouth, by muscle, by vein in the handling of all types of human pathology either as the specific drug or as an adjuvant with other antibiotics or neutralizing chemicals. In severe pathological conditions the urine sample, taken every four hours, must show a fine charcoal-like precipitation with a clear supernatant liquid if positive clinical results are to be realized. Spilling in the urine is not new. Abraham and Keefer have demonstrated that when penicillin is injected intravenously, excretions in the urine account for 60 percent of the administered dose.

Role played by ascorbate in intercellular reactions, neutralizing, possibly controlling virus production

In 1935 Stanley isolated a crystalline protein possessing the properties of tobacco mosaic virus. It contained two substances, ribonucleic acid (**RNA**) and protein. The simple structure characteristic of tobacco mosaic virus was soon found to be a basic property of many human viruses such as **coxsackie virus** (which I believe to be the cause of **Multiple Sclerosis**), **Echoviruses** and **polioviruses** — they all contain only ribonucleic acid and protein. There exist minor variations. Adenoviruses contain deoxyribonucleic acid (**DNA**) and protein. Other viruses such as that causing **influenza** contain added lipid and polysaccharides. Deoxyribonucleic acid is used to program the large viruses, like mumps, ribonucleic acid is used to program the small viruses, like measles. The role of the protein coat is to protect the parasitic but unstable nucleic acid as it rides the “blood highway” or “lymphatic system” to gain specific cell entry. Pure viral nucleic acid without its protein coat can be inactivated by constituents of normal blood. There are several theories as to what happens after cell entry:

- Once inside a given cell, the virus nucleic acid sheds its protein coat and proceeds to modify the host cell by either creating mutations or by directly substituting its own nucleic acid;

- The infectious nucleic acid, after entering a human cell, retains its protein coat and starts to produce its own type protein coat[16] and viral nucleic acid, so that new units can either depart to enter other cells or by destruction of the cell, thus making the infection more severe;
- The introduction of a foreign fragment of nucleic acid in the cell-virus interaction approach as postulated by Starr[17]. In the Starr theory there can exist cells with partial chromosome make-up and cells with multi-nuclei. Hiliary Kropowski holds that these partial cells are ‘pseudo-virons’[18] and are found in some tumor-virus infections. A key factor in the Starr-Kropowski thinking is that the cell maintains its biological integrity to support virus development despite the abnormal morphology and genetic deficiency. If these invaded cells could be destroyed or the invader neutralized the illness would suddenly terminate. Ascorbate has the capability of entering all cells. Under normal circumstances its presence is beneficial to the cell, however, when the cell has been invaded by a foreign substance, like virus nucleic acid, enzymatic action by ascorbate contributes to the breakdown of virus nucleic acid to adenosine deaminase which converts adenosine to inosine. The net result is to lead to purines which are extensively catabolized and not to p+urines which are utilized for further nucleic acid. Ascorbate also joins with the available virus protein, making a new macromolecule which acts as the repressor factor. It has been demonstrated that when combined with the repressor, the operator gene, virus nucleic acid, cannot react with any other substance and cannot induce activity in the structural gene, therefore inhibiting the multiplication of new virus bodies. The tensile strength of the cell membrane is exceeded by these macromolecules with rupture and destruction. Another hypothesis is that vitamin C acts to create new “L” viruses which are impotent. Still another, that the “binding” alone is sufficient to destroy the virus.

Promptness of massive ascorbate in avoiding fatal encephalitis related to stubborn head and chest colds

In 1953[19] we presented a case history and films of a patient with **virus pneumonia**. This patient was unconscious, with a fever of 106.8°F (A. corrected) when admitted to the hospital. 140 grams ascorbate was given intravenously over a period of 72 hours at which time she was awake, sitting up in bed and taking fluids freely by mouth. The temperature was normal. Since that time we have observed a more deadly syndrome associated with a virus causing head and chest colds. This is one of the adenovirus striking in the area of the upper respiratory tract with resulting fever, sore throat and eyes, and when in children can cause fatal pneumonia. More often death is indirect by way of incipient **encephalitis** where the child can be dead in 30 minutes. These are the babies and children found dead in bed and attributed to suffocation [**SIDS, Sudden Infant Death Syndrome**]. It is suffocation but by way of a syndrome we observed and reported in 1957[20] which is similar to that found in cephalic tetanus-toxemia culminating in diaphragmatic spasm, with dyspnea and finally asphyxia.[21] By 1958[22] we had collected sufficient information from our office and hospital patients to catalog this deadly syndrome into two important stages.

- Stage 1
 - There is always a history of having had the **“Flu” which lasted 48 to 96 hours** complicated with extreme physical or mental distress; or
 - A mild **cold, similar to an allergic rhinitis, which lingered on for several weeks** but did not incapacitate the individual.
- Stage 2, which is always sudden, will present itself in at least seven forms:
 - Convulsive seizures;
 - Extreme excitability resembling delirium tremens if an adult and with dancing of the eyeballs if a child;
 - Severe chill;
 - Strangling in the course of eating or drinking (bulbar type);
 - Collapse;
 - Stupor;
 - Hemiplegic type.

Other findings of this dramatic second stage are:

- Rapid pulse;
- Temperature can be normal, moderately elevated or high;
- Respirations twice to three times normal and in some cases will be suggestive of air hunger;
- Pupils will be moderately open and in some instances (hemiplegic) one will be markedly dilated;
- Urine negative;
- The white blood count running from 6,000 to 25,000 with a high poly count in the differential;
- Young patients starting the second phase with a convulsion when there has been not only a history of normal bowel movements but also when an enema given at the time of first examination has produced a normal stool;
- Bladder sphincter control was abnormal in our cases who convulsed or who were in coma.

Neurological Changes

It is apparent that the second stage of this syndrome is triggered by a breakthrough at the site of **the blood-brain barrier**. The time required for neurological changes to become evident is roughly comparable to the time necessary for similar neuropathology to be demonstrated following a **severe head injury**. Cerebral edema exists in both conditions. In my practice I start massive ascorbate therapy immediately. I have seen **children dead in from 30 minutes to 2 hours** because their attending physician was not impressed with their illness upon hospital admission. An autopsy on one of these patients showed **bilateral pneumonitis** — all one needs to spark a **deadly encephalitis**. To indicate just how common this syndrome presents itself, I relate here a newspaper account of a 15 year old girl who had a **mild, lingering cold** for several weeks. She attended a dance party one evening and except for a complaint of feeling extremely tired, she went to bed apparently well. She was found dead in bed the following morning. An autopsy showed bilateral pneumonia. How many times have you read such an account? This is why it is necessary for everybody to take adequate supplemental vitamin C to guard against such disasters.

Literature Research

In 1960 we decided to research the literature before writing our paper. “**Virus Encephalitis As A Sequel Of The Pneumonias.**”[[22](#)] Rosenfield in 1903 described a similar syndrome under the caption “Brain Purpura or Hemorrhagic Encephalitis.” Comby, in 1907, was the first to call attention to the interesting “metastatic” sequela of the pneumonias. Baker and Noran in 1945 enumerated five groups, each showing certain definite clinical characteristics which may be of both diagnostic and prognostic significance in relation to this virus syndrome.[[23](#)]

- Symptoms of a nonspecific nature – headache, vomiting, irritability;
- Delirious type;
- Convulsive type;
- Lethargic type;
- Hemiplegic type.

These groups plus two additional types, namely:

- Chill – blood invasion type;
- Collapse,

were as we reported them, independently, in the Tri-State Medical Journal, October 1958. Their results: **Some recovered, some died and still others lived as “vegetation” mental cripples. All of our patients recovered.** Thirteen years from the time of the Baker-Noran report to the time of our report and 13 years from the time of our report to the present time. This makes the issue urgent. Physicians must recognize the

inherent danger of the lingering head or chest cold and appreciate the importance of early massive vitamin C therapy.

How does the brain become involved in encephalitis? — some speculations

Clinical problems such as these groups present, lead one to speculate on the pathways in which the virus gains entrance into the brain. We can summarize:

- Through the olfactory nerves;
- Through the portals of the stomach from material swallowed, either pulmonary or upper respiratory drainage;
- Direct extension from otitis media or from mastoid cells;
- The blood stream. Arriving in the brain the virus goes through the blood cerebrospinal fluid barrier and/or the blood brain barrier by one of three ways:
 - Electrical charge;
 - Chemical lysis of tissue;
 - Osmosis.

Bakay[24] reported that the **permeability of the blood-brain barrier** can be changed by introducing various toxic agents into the blood circulation. Chambers and Zweifach[25] emphasized the importance of the intercellular cement of the capillary wall in regulating permeability of the blood vessels of the central nervous system. In this syndrome the toxic substance is an **adenovirus**. Ascorbate will repair and maintain the **integrity of the capillary wall**.

Burns – degrees explained and some therapy rational

In the **treatment of burns** ascorbate, in sufficient amounts, reflects itself as a truly miracle substance. In the early forties, when I was using ascorbate, intramuscularly, in treating **bacillary dysentery**, shiga type, with excellent results, Lund, Lam and many others were using, what they called, massive doses of ascorbate in the treatment of burns. One or two grams each day, in fluids, was the recognized dose. Burns are at the beginning first degree and some remain as just an erythema. Many times the **first degree burn progresses rapidly** to the second degree stage and remains as “blisters”. Still others go on to **third degree** which usually is more pronounced on the third-plus post-burn day. There is a **fourth stage** which results from lack of knowledge in treatment. It terminates with **skin grafting and plastic surgery**. We believe that ascorbate will eliminate the fourth stage and the third stage if used as we will later program.

Burns – continued descriptive and related therapies

The pathologic **physiology of a burn wound** from the moment of the accident is in a state of dynamic change until the wound heals or the patient dies. The primary consideration is the phenomenon of blood sludging originally recognized by Knisely in 1945.[26,27] Initially there is intravascular agglutination of red blood cells into distinctly visible, smooth, hard, rigid, basic masses. Lofstrom in 1959 demonstrated that the **oxygen uptake** by the tissues is greatly reduced because of the sludging and therefore reduced rate of flow. Berkeley[28] in 1960 concluded that this phenomenon of sludging or agglutination results in capillary thrombosis in the area of the burn, extending proximally to involve the large arterioles and venules and thereby creating tissue destruction greater than that originally produced by the burn. Anoxia produces **added tissue destruction**. Lund and Levenson[28] found that after severe burns there is considerable alteration in the metabolism of ascorbate as shown by a low concentration of ascorbate in the plasma either with the patient fasting or after saturation tests and also low urinary excretion of vitamin C either with the patient fasting or after the injection of test doses. The extent of the abnormality closely paralleled the severity of the burn. Bergman[30] reported an increase demand for ascorbate in burns especially when epithelization and formation of granulation tissue are taking place. Lam[31] also reported in 1941 a marked decrease in the plasma ascorbate concentration in patients with severe burns. Klasson[32]

although limiting the amount of ascorbate to a dose range of 300 mg to 2000 mg daily, in divided doses, found that it hastened the healing of wounds by producing healthy granulation tissue and also that it reduced local edema. He rationalized that **ascorbate used locally** as a 2% dressing possessed astringent properties similar to hydrogen peroxide. He also reported that **antibiotic therapy was rarely necessary**.

Severe burns and related therapy

Harlen Stone^[33] suggested the use of gentamicin in major burns to lower the sepsis caused by pseudomonas. Absorption of its exotoxin from the infected burn wound inhibits the bacterial defense mechanism of the reticuloendothelial system. Death can result either from the toxemia alone or from an associated septicemia. We have found that the secret in treating burns can be summarized in five steps:

1. The use of the “old covered wagon” type cradle when indicated, with three 25 watt bulbs. The patient controls the heat by turning on and off the first bulb as needed to keep warm. No garments or dressings are allowed;
2. The employment of a 3% ascorbate solution as a spray over the entire area of the burn. The spray can be applied with a Devilbis unit using an ordinary portable pressure pump. The old type “flit gun” can also be used or even a 50 c.c. syringe with a 20 gauge needle. The 3% solution is used every 2 to 4 hours for a period of roughly five days;
3. The use of vitamin A and D ointment over the area of the burn and this is now alternated, q4h with the 3% ascorbate solution;
4. The administration of massive doses of ascorbate by vein and by mouth. 500 mg per Kg. body weight diluted to at least 18 c.c. per gram vitamin C [sodium ascorbate] using 5% dextrose in water, saline in water or Ringers solution and for the initial injection, run in as fast as a 20 gauge needle or catheter will carry the flow. Cut-downs are frequently necessary and the foot-ankle area is recommended. Vitamin C [sodium ascorbate] solution is repeated every 8 hours for the first several days, then at 12 hour intervals. Ascorbate, by mouth, is given to tolerance. Loose stools is accepted as this index. Using large doses of ascorbate I.V. will necessitate the administration of at least one gram **calcium gluconate**, daily, to replace free calcium ions removed in the breakdown chemical action as ascorbate goes to dehydroascorbate, then to ketogulonic acid and later to oxalic acid as the calcium salt;
5. Supportive treatment; that is, whole blood and maintaining electrolyte balance.

If seen early after the burn there will be no infections and no eschar formations. This eliminates fluid formation, since the eschar traps will not exist and there will be no distal edema because the venous and lymphatic systems will remain open. There will be no arterial obstruction and no nerve compression. Pseudomonas will not be a problem, since ascorbate destroys the exotoxin systemically and locally. Even if the burn is seen late when pseudomonas is a major problem the gram negative bacilli will be destroyed in a few days leaving a clean healthy surface. I have seen **eschars** 2 inches wide and 1/2 inch thick, severely infected so that stench had to be controlled with deodorizing sprays, **melt away** when employing the method outlined. Ascorbate also eliminates pain so that **opiates or their equivalent are not required**. In extremely extensive burns that involve back and front of the patient, the “**Hoverbed**”^[35] employed by the British should be considered. It uses the same principle as the hovercraft to lift a solid object. What has been overlooked in burns is that there are many living epithelial cells in the areas that grossly look like “raw muscle.” With the use of ascorbate these cells are kept viable, will multiply and soon meet with other proliferating units in the establishment of a new integument.

Regarding personal and environmental pollution – carbon monoxide

We are all plagued with varying degrees of chronic **carbon monoxide poisoning**. This is the price we pay for putting our “railroads” on our highways, **smoking** and being too lazy to walk. Small amounts of carbon monoxide, if constantly maintained in the alveoli, can produce serious effects. Carbon monoxide in the inspired air leads to oxygen deficiency in the tissues causing extreme exhaustion. The affinity of carbon monoxide for hemoglobin is roughly **300 times** as great as that for oxygen. In addition to active

replacement of oxy-hemoglobin the presence of some proportion of carboxy-hemoglobin decreases the dissociability of such oxy-hemoglobin as remains. Carbon monoxide can be released from hemoglobin if the patient is exposed to high pressure of oxygen, 93% along with 7% carbon dioxide. This is not always available. Ascorbate in the blood is constantly losing molecules of water. Perfectly dry carbon monoxide and oxygen cannot unite to form carbon dioxide, but carbon monoxide and water may give rise to carbon dioxide in the complete absence of oxygen. The reactions which take place are



Here the oxygen of the water has been used to oxidize carbon monoxide to carbon dioxide with the liberation of hydrogen. **Glutathione** may facilitate this cellular oxidation by acting as a hydrogen acceptor (Hopkins). Clinical experience suggests that if sufficient ascorbate is suddenly placed into the blood stream — 12 grams to 50 grams — that through “**Flash Oxidation**” a concentration of oxygen is made high enough to pull carbon monoxide from hemoglobin to form carbon dioxide. This rapidly formed carbon dioxide acts with the high oxygen tension to serve the same purpose as when given by “mask,” further enhancing the chemical action taking place. Ascorbate will also prevent residuals such as paralysis, blindness, interference with sensations, muscle spasms or twitchings which in some cases can be permanent.

Primary and lasting benefits in pregnancy

Observations made on over 300 consecutive obstetrical cases using supplemental ascorbate, by mouth, convinced me that failure to use this agent in sufficient amounts in pregnancy borders on malpractice. The lowest amount of ascorbate used was 4 grams and the highest amount 15 grams each day. (Remember the rat—no stress manufactures equivalent “C” up to 4 grams and with stress up to 15.2 grams). Requirements were roughly 4 grams first trimester, 6 grams second trimester and 10 grams third trimester. Approximately 20 percent required 15 grams, each day, during last trimester. Eighty percent of this series received a booster injection of 10 grams, intravenously, on admission to the hospital. Hemoglobin levels were much easier to maintain. **Leg cramps** were less than three percent and always was associated with “getting out” of Vitamin C tablets. **Striae gravidarum** [stretch marks] was seldom encountered and when it was present there existed an associated problem of too much eating and too little walking. The capacity of the skin to resist the pressure of an expanding uterus will also vary in different individuals. Labor was shorter and less painful. There were no postpartum hemorrhages. The perineum was found to be remarkably elastic and episiotomy was performed electively. Healing was always by first intention and even after 15 and 20 years following the last child the firmness of the perineum is found to be similar to that of a primigravida in those who have continued their daily supplemental vitamin C. No patient required catheterization. No toxic manifestations were demonstrated in this series. There was no cardiac stress even though 22 patients of the series had rheumatic hearts. One patient in particular was carried through two pregnancies without complications. She had been warned by her previous obstetrician that a second pregnancy would terminate with a maternal death. She received no ascorbate with her first pregnancy. This lady has been back teaching school for the past 10 years. She still takes 10 grams of ascorbate daily. Infants born under massive ascorbate therapy were all robust. Not a single case required resuscitation. We experienced no feeding problems. The Fultz quadruplets were in this series. They took milk nourishment on the second day. These babies were started on 50 mg ascorbate the first day and, of course, this was increased as time went on. Our only nursery equipment was one hospital bed, an old, used single unit hot plate and an equally old 10 quart kettle. Humidity and ascorbate tells this story. They are the only quadruplets that have survived in southeastern United States. Another case of which I am justly proud is one in which we delivered 10 children to one couple. All are healthy and good looking. There were no miscarriages. All are living and well. They are frequently referred to as **the vitamin C kids**, in fact all of the babies from this series were called “**Vitamin C Babies**” by the nursing personnel—they were distinctly different.

How concerned should we be about oxalic acid and kidney stones? A technical explanation

One of the “scare” weapons used by the critics on high daily doses of ascorbate is the oxalic acid-**kidney stone** hypothesis. Meakins[36] states that the chief factors in the formation of renal calculi are perversions of metabolic processes, infection and stasis in the urinary tract. There are two schools of thought on stone formation: 1) That there is a central nucleus of colloids on which the crystalloids are precipitated; 2) That the crystalloids are deposited from the urine in which they are present in concentrated solution, in which salt and hydrogen ion concentrations are important factors. In all cases stasis and a concentrated urine appear to be the chief physiological factors. The only way that oxalic acid can be produced from ascorbate is through splitting of the lactone ring. This happens above pH5. The reaction of urine when 10 grams of vitamin C is taken daily is usually pH6. Oxalic acid precipitates out of solution only from a neutral or alkaline solution – pH7 to pH10. Kelli and Zilva[37] reported that “Nutrition experiments showed that dehydroascorbate is protected in vivo from rapid transformation to the antiscorbutically impotent diketogulonic acid from which oxalic acid is derived.” Values reported in the literature for normal 24 hour urinary oxalate excretions for humans range from 14 mg to 56 mg. Lamden et al.[38] found in a group of volunteers that the ingestion of 9 grams ascorbate daily resulted in oxalate spills as high as 68 mg for 24 hours and in the controls without extra vitamin C the high was 64 mg for a 24 hour period.

These critics have overlooked the individual with **diabetes mellitus**. The amount of oxalic acid found in the diabetic patient approximates that found in the urine of a normal person taking 10 grams vitamin C each day. With the diabetic we find a paradox. Give this individual 10 grams ascorbate daily, by mouth, and the urinary oxalate excretion remains relatively unchanged. Diabetics are known for their diuresis. The individual who takes 10 or more grams of vitamin C each day will find that this organic compound is an excellent diuretic. No urinary stasis; no urine concentration.

The ascorbate kidney stone story is a myth. Methylene blue will dissolve calcium oxalate stones giving 65 mg orally 2 to 3 times a day. (Dr. M. J. Vernon Smith: Med. World News, Dec. 4, 1970)

Why death from insect and snake bites?

It is estimated that 6500 deaths occur each year in the United States from snake **bite**. Many more from various flying insects, spiders, certain plants and some caterpillars. These are needless deaths. Several factors are at work in these pathologies:

- The tox-albumin of the snake bite, like the copperhead or rattler;
- Formic acid plus a toxin with a protein cover, called proteotoxin by Arthus,[39] such as found in bees and wasps;
- Neurotoxin from the Black Widow, the Fiddle Spider and snakes like the Cobra and Coral;
- Production of histamine, especially in the more severe stings and bites.

Wells[40] in 1925 called the poison of certain spiders and snakes **zootoxins** and of poisonous plants, **phytotoxins**. Ford[41] in 1911 reported three classes of toxins in plants and fungi:

- Nerve poisons—muscarine;
- Those causing structural changes in the viscera with resulting fatty degeneration;
- Gastrointestinal irritants.

Ascorbate to the rescue

It is a demonstrated principle that the production of **histamine** and other end products from deaminized cell proteins released by injury to cells are a cause of **shock**. The clinical value of ascorbate in combating shock is explained when we realize that the deaminizing enzymes from the damaged cells are inhibited by vitamin C.[42] It has been shown by Chambers and Pollock[43] that mechanical damage to a cell results in pH changes which reverse the cell enzymes from constructive to destructive activity. The pH changes spread to

other cells. This destructive activity releases histamine, a major shock producing substance. The presence of vitamin C inhibits this enzyme transition into the destructive phase. Clark and Rossiter[44] reported that conditions of shock and stress cause depletion of the ascorbate content of the plasma. As with the virus bodies, ascorbate also joins with the protein factor of these toxins effecting quick destruction.

The answer to these emergencies is simple. Large amounts of ascorbate 350 mg to 700 mg per Kg. body weight given intravenously. In small patients, where veins are at a premium, ascorbate can easily be given intramuscularly in amounts up to two grams at one site. Several areas can be used with each dose given. Ice held to the gluteal muscles until red, almost eliminates the pain. We always reapply the ice for a few minutes after the injection. Ascorbate is also given, by mouth, as follow-up treatment. Every emergency room should be stocked with vitamin C ampoules of sufficient strength so that time will never be counted as a factor in saving a life. The 4 gram, 20 c.c. ampoule and 10 gram 50 c.c. ampoule must be made available to the physician.

A case history – success due to promptness with a twelve gram injection

As an example of the lethal effect of certain stings and bites, I briefly relate a case history. An adult male came to my office complaining of severe chest pain and the inability to take a deep breath. Stated that he had been “stung” or “bitten” 10 minutes earlier. Thinking that it was a Black Widow and not bothering to look for fang marks, due to the gravity of the situation, I gave one gram calcium gluconate intravenously. This gave no relief. He begged for help saying **he was dying**. He was becoming cyanotic [blue or livid skin from lack of oxygen]. Twelve grams of vitamin C was quickly pulled into a 50 c.c. syringe and with a 20 gauge needle was given intravenously as fast as the plunger could be pushed. Even before the injection was completed, he exclaimed, “Thank God”. The poison had been neutralized that rapidly. He was sent home to locate the “culprit”. He soon returned with an object that looked like a mouse. It was 1 1/2 inches long with long brown hair. There was a dark ridge down the entire back. It had seven pairs of propelling units and a tail much like a mouse. The following day I took “The Thing” to Duke University where it was identified as the **Puss Caterpillar**. This unusual caterpillar left 44 red raised marks on the back of its victim. Except for vitamin C this individual would have died from shock and asphyxiation.

Some concern answered regarding high dosage of ascorbate

Merton Lamden, a biochemist, writing in the New England Journal of Medicine, Feb. 11, 1971, expresses grave doubts about the safety of large doses of ascorbate taken by mouth. He gives a report by Paterson[45] on the diabetogenic effect of dehydroascorbate on rats. Paterson in 1950 employed only the Ketone formula of ascorbate, dehydroascorbate, which he administered, undiluted, intravenously, in extraordinary amounts. His results were based on giving rats weighing 100 grams to 120 grams dehydroascorbate in doses from 20 to 50 mg. This transposed to a man weighing 70 kilograms would represent a dose of 3,500 grams—roughly 5,000 grams ascorbate. Obviously the work has no relationship with the ingestion of ascorbate by humans. I have taken from 10 to 20 grams of ascorbate daily since my last visit to this college — 18 years ago. I do not have diabetes mellitus and if I might digress a moment, neither have I had a kidney stone.

Diabetes mellitus response to 10 grams ascorbate by mouth

Over the past 17 years we have studied the effect of 10 grams by mouth, in patients with diabetes mellitus. We found that every diabetic not taking supplemental vitamin C could be classified as having **sub-clinical scurvy**. For this reason they find it **difficult to heal wounds**. The diabetic patient will use the supplemental vitamin C for better utilization of his insulin. It will assist the liver in the metabolism of carbohydrates and to reinstate his body to heal wounds like normal individuals. We found that 60% of all diabetics could be controlled with diet and 10 grams ascorbate daily. The other 40% will **need much less needle insulin** and less oral medication. Contrary to what Medical News Letter, (Vol. 12 # 26, Dec. 25 1970) carried to the physicians the Tes-Tape is accurate in testing urine samples.

Observations following post-surgery cases on blood plasma levels of ascorbate. Deduction is evident of the need for substantial amounts of ascorbate prior to surgery.

In 1960 and again in 1966, in papers delivered before the Tri-State Medical Society, I called attention to the “**scurvy**” levels of ascorbate found in **postoperative** patients. Plasma levels recorded before starting anesthesia and after cessation of such inhalants and completion of surgery remained unchanged. This has led many to believe that surgery created little or no demand for supplemental “C”. We found, however, that samples of blood taken six hours after surgery showed drops of approximately 1/4 the starting amount and at 12 hours the levels were down to one-half. Samples taken 24 hours later, without added ascorbate to fluids, showed levels 3/4 lower than the original samples. A Baylor University research team reported similar findings in 1965. Bartlett, Jones[48] and others reported that in spite of low levels of plasma ascorbate at time of surgery, normal wound healing may be produced by adequate vitamin C therapy during the post-operative period. Lanman and Ingalls[47] showed that the tensile strength of healing wounds is lowered in the presence of “scurvy plasma levels”. Schumacher[48] reported that the preoperative use of as little as 500 mg of vitamin C given orally “was remarkably successful in preventing shock and weakness” following dental extractions. Many other investigators have shown in both laboratory and clinical studies, that optimal primary wound healing is dependent to a large extent upon the vitamin C content of the tissues.

In 1949, it was my privilege to assist at an abdominal exploratory laparotomy. A mass of small viscera was found “glued together”. The area was so friable that every attempt at separation produced a torn intestine. After repairing some 20 tears the surgeon closed the cavity as a **hopeless situation**. Two grams ascorbate was given by syringe every two hours for 48 hours and then 4 times each day. In 36 hours the patient was walking the halls and in seven days was discharged with normal elimination and no pain. She has outlived her surgeon by many years. We recommend that all patients take 10 grams ascorbate each day. Where this is not done and the surgery is elective, then 10 grams by mouth should be given for several weeks prior to surgery. At least 30 grams should be given, daily, in solutions, post-operatively, until oral medication is allowed and tolerated.

Mononucleosis aided by ascorbate

After studying hundreds of college students, Yale researchers have evidence that strengthens the link between mononucleosis and **Epstein-Barr virus**, a herpes-like agent also associated with **Burkitt lymphoma**. [49] Large doses of intravenous “C” has a striking influence on the course of **mononucleosis**. In one patient who was given the last rites of her church, the girl’s mother took things into her own hands when the attending physician refused to give ascorbate. In each bottle of intravenous fluids she would quickly “tap in” 20 to 30 grams vitamin C. The patient made an uneventful recovery. Her mother has her B.S. in Nursing and has been a long time advocate of massive “C” therapy.

Could ascorbate have anti-cancer features?

Schlegel[50] from Tulane University has been using 1.5 grams ascorbate daily to prevent recurrences of **cancer of the bladder**. He and biochemist Pipkin have been able to demonstrate that in the presence of ascorbate, carcinogenic metabolites will not develop in the urine. They suggest that spontaneous tumor formation is the result of **faulty tryptophan metabolism** while urine is retained in the bladder. Schlegel termed ascorbate “**An Anticancer Vitamin**”. Along this line Glick and Hosoda[51] reported on work by Von Numers and Pettersson that the depletion of mast cells from guinea pigs skin was due to ascorbate deficiency. The possibilities indicated are that vitamin C is necessary either directly or indirectly for formation of mast cells, or for their maintenance once formed or both. Ascorbate will control myelocytic leukemia provided 25 to 30 grams are taken orally each day.

One can only speculate on what massive therapy would do in all forms of cancer. Many pathologic conditions are cured by giving 5 million to 100,000 million units of penicillin as an intravenous drip over a period of 4 to 6 weeks. How long must we wait for someone to start continuous ascorbate drip for 2 to 3 months, giving 100 to 300 grams each day, for various malignant conditions?

Barbiturate patients in shock normalized with ascorbate

Clemmesen[52] states that the important principles in management of barbiturate poisoning are anti-shock therapy, continuous oxygen and patent airways. Hadden et al.[53] suggest six measures as supportive treatment. An intensive care unit would be necessary to carry out these functions. All one really need do is give adequate ascorbate therapy. One patient who had taken 2640 mg **Lotusate** (talbutal) was seen in the emergency room with a blood pressure of 60/0. Twelve grams vitamin C was given intravenously with a 50 c.c. syringe and then the needle attached to a bottle of 5D water containing 50 grams ascorbate. Within 10 minutes the blood pressure was 100/60 demonstrating the effect of vitamin C on shock. A second bottle of 250 c.c. 5D water containing one gram emivan was started in the other arm. The patient was awake in 3 hours, taking juice with "C" added. She received 125 grams ascorbate by vein in 12 hours. Ascorbate not only assists with hepatic metabolism but also as a major diuretic flushes these compounds out by way of the kidneys. Nasal oxygen running 6 liters per minute was also employed. Another patient who had masked 2400 mg seconal with paraldehyde was awake after 42 grams of ascorbate had been given by vein as fast as a 20 gauge needle could carry the flow. She received 75 grams vitamin C by vein and 30 grams by mouth in a 24 hour period.

Cholesterol not a problem, when daily intake of ascorbate is high

Mention should be made of the role[54] played by vitamin C as a regulator of the rate at which cholesterol is formed in the body; deficiency of the vitamin speeding the formation of this substance. In experimental work, guinea pigs fed a diet free of ascorbate showed a 600 percent acceleration in cholesterol formation in the adrenal glands. Ten grams or more each day and then eat all the eggs you want. That is my schedule and my cholesterol remains normal, Russia has published many articles demonstrating these same benefits.

Lockjaw relieved

Ascorbate has no equal as an adjuvant with other drugs in many conditions. With **Tolserol** it is curative in the treatment of Lockjaw. Both drugs must be used in proper amounts. In our case 1000 mg Tolserol given intravenously to a boy weighing 20 Kg. was the optimal amount to use. In 48 hours he was given 90 grams ascorbate and 3000 mg Tolserol, all intravenously.[55] Jungeblut[56] reported that vitamin C, when added to tetanus toxin "in vitro", brings about inactivation of the toxin.

Two cases of **Trichinosis** were treated and cured using Vitamin C and Para-Aminobenzoic acid.[57] Although the temperature curve was returned to normal in 36 hours it was found that nine days of treatment were necessary for permanent cures.

Infectious hepatitis relieved

Viral hepatitis needs brief mentioning. There are two types: 1) Infectious hepatitis; 2) Needle hepatitis. Physical activity has always been considered to increase the severity and prolong the course of the disease.[58] In Vietnam, Freebern and Repsher showed that pick-and-shovel details had no effects on the 199 controls as against 199 kept at bed rest.[59] One thing is certain. Give massive intravenous ascorbate therapy and patients are well and back to work in from 3 to 7 days. In these cases the vitamin is also employed by mouth as follow-up therapy. Dr. Bauer at the University Clinic, Basel, Switzerland, reported that just 10 grams daily, intravenously, proved the best treatment available.

Ascorbate therapy applied to various maladies

We could continue indefinitely extolling the merits of ascorbate.

- Boyd and Campbell[60] reported excellent results in the healing of **corneal ulcers** even though their massive doses was 1.5 grams daily. In one case of a corneal burn from the phosphorus off an old time match, the pain was relieved immediately with the intravenous injection of 12 grams vitamin C with a 50 c.c syringe. One gram was prescribed each hour for 50 grams. The cornea was normal in less than 24 hours.
- One single injection of ascorbate calculated at 500 mg per Kg. body weight will reverse **heat stroke**.
- One to three injections of the vitamin in a dose range of 400 mg Kg. body weight will effect a dramatic cure in **Virus Pancarditis**.
- One gram taken every one to two hours during exposure will prevent **sunburn**.
- Intravenous injections will quickly relieve **sunburn** pain and **erythema**, even the second degree burns when precautions are not taken.
- One to three injections of 400 mg per Kg. given every eight hours will “dry up” **chicken-pox** in 24 hours.
- If **nausea** is present it will stop the nausea.

These injections are usually given with a syringe in a dilution of one gram to 5 c.c fluid. This concentration will produce immediate thirst. This is prevented by having the patient drink a glass of juice just before giving the injection.

- 40 grams ascorbate by vein and 1000 mg to 2000 mg vitamin B1 intramuscularly will neutralize the person **intoxicated by alcohol** and will **save the life** if one drinks after using **Antibuse**.
- 5 per cent ointment using a water soluble base will cure acute **fever blisters** if applied 10 or more times a day and we have removed several small **basal cell epithelioma** has with a 30 percent ointment.
- Dr. Virno[61] at the eye clinic, University of Rome, Italy, reported very promising results in **glaucoma** with a dose schedule of 100 mg per Kg. body weight taken after meals and bed hour. He also reported that these large doses have proved to be safe.
- In **arthritis** at least 10 grams daily and those taking 15 to 25 grams daily will experience commensurate benefit. Supportive treatment must also be given. Repair of collagenous tissue is dependent of adequate ascorbate.
- Complications of **smallpox vaccination** are usually handled by adequate oral ascorbate. Several times we found it necessary to give the “C” intravenously along with Adenosine. Twenty percent ichthammol used locally with vaccinia necrosum is good psychology.
- In **herpes zoster** two grams vitamin C intramuscularly and 50 mg Adenosine 5-Monophosphoric acid, aqueous solution, also intramuscularly every 12 hours. Compound tincture benzoin locally is helpful.
- In massive “**shingles**” ascorbate should also be given by vein. Always as much by mouth as can be tolerated.
- **Heavy metal intoxication** is resolved with adequate vitamin C therapy.

General all around benefits of one to ten grams ascorbate per day

It has been suggested that ascorbate metabolism may be an index of total metabolism and thus serve as a general diagnostic guide. Adults taking at least 10 grams of ascorbate daily, and children under ten at least one gram for each year of life will find that the **brain will be clearer**, the mind more active, the body less wearied and the memory more retentive.

Summary

The types of pathology treated with massive doses of ascorbate run the entire gamut of medical knowledge. Body needs are so great that so-called **minimal daily requirements must be ignored**. A genetic error is the probable cause for our inability to manufacture ascorbate, thus requiring exogenous sources of vitamin C. Simple dye or chemical tests are available for checking individual needs. Ascorbate destroys virus bodies by taking up the protein coat so that new units cannot be made, by contributing to the breakdown of virus nucleic acid with the result of controlled purine metabolism. Its action in dealing with virus pneumonia and virus encephalitis has been outlined. The clinical use of vitamin C in pneumonia has a very sound foundation. In experimental tests monkeys kept on a vitamin C free diet all died of pneumonia while those with adequate diets remained healthy.[62] Many investigators have shown an increased need for ascorbate in this condition.[63,64] Brody in 1953 after studying vitamin C and colds in college students advised that ascorbate be given early and often in sufficient amounts. Regnier[65] reporting in Review of Allergy found that the larger the dose of ascorbate the better were the results. Our findings resulted in a schedule of one gram each hour for 48 hours and then 10 grams each day by mouth. Those under ten at least one gram for each year of life.

Virus Encephalitis.

Virus encephalitis is a deadly syndrome and must be treated heroically with intravenous and/or intramuscular injections of ascorbate. We recommend a dose schedule of from 350 mg to 700 mg per Kg. body weight diluted to at least 18 c.c. of 5D water to each gram of "C". In small children, 2 and 3 grams can be given intramuscularly, every 2 hours. An ice cap to the buttock will prevent soreness and induration. Ascorbate in amounts under 400 mg per Kg. body weight can be administered intravenously with a syringe in dilutions of 5 c.c. to each one gram provided the ampoule is buffered with sodium bicarbonate with sodium Bisulfite added. As much as 12 grams can be given in this manner with a 50 c.c. syringe. Larger amounts must be diluted with "bottle" dextrose or "saline" solutions and run in by needle drip. This is true because amounts like 20 to 25 grams which can be given with a 100 c.c. syringe can suddenly dehydrate the cerebral cortex so as to produce convulsive movements of the legs. This represents a peculiar syndrome, symptomatic epilepsy, in which the patient is mentally clear and experiences no discomfort except that the lower extremities are in mild convulsion. This epileptiform-type seizure will continue for 20 plus minutes and then abruptly stop. Mild pressure on the knees will stop the seizure so long as pressure is maintained. If still within the time limit of the seizure the spasm will reappear by simply withdrawing the hand pressure. I have seen this in two patients receiving 26 grams intravenously with a 100 c.c. syringe on the second injection. One patient had poliomyelitis, the other malignant measles. Both were adults. I have duplicated this on myself to prove no after effects. Intramuscular injections are always 500 mg to 1 c.c. solution. With continuous intravenous injections of large amounts of ascorbate, at least one gram of calcium gluconate must be added to the fluids each day. This is done because we have found that massive doses of ascorbate pulls free calcium ions from the vicinity of the platelets or from the calcium-prothrombin complex as the lactone ring of dehydroascorbate is opened. The first sign of calcium ion loss is "nose bleeding". This differs from the nosebleed found, at times, in cases of chicken pox or measles. Here it represents frank scurvy from vitamin C deficiency. The pathology being "**Capillary fragility**".[66]

Burns

A new treatment for burns has been outlined, which if followed will eliminate skin grafting and plastic surgery. It is probably too simple to gain early acceptance. The literature has been suggesting the value of ascorbate in burns for many years. Proper local application and the amount for systemic usage has been misleading. One only need see one case properly treated with ascorbate to appreciate its importance. If ascorbate can destroy the exotoxin of tetanus, as Jungeblut demonstrated, it can also destroy the exotoxin of Pseudomonas. Ascorbate plays an important role in maintaining fluid balance in the body. Ruskin pointed out that the vitamin activates the enzyme arginase, which breaks down the amino acid arginine, resulting in production of urea which is one key to tissue fluid balance.

Pregnancy

The simple stress of pregnancy demands supplemental vitamin C. This amount will vary with the individual. The silver nitrate-urine test will simplify these findings. Vitamin C seems especially concerned with **mesenchymal tissue**. When one considers the demands of the fetus and infant, especially premature babies, it is obvious that high vitamin C intakes are required during pregnancy because this “parasite” will drain available “C” from the mother. Greenblatt[67] reports excellent results following the oral administration of vitamin C in the therapy of habitual abortion. In my own practice I was able to take women who had had as many as five abortions without a successful pregnancy and carry them through two and three uneventful pregnancies with the use of supplemental vitamin C. The German literature is “stacked” with articles recommending high doses of vitamin C during gestation because they believe that this substance is of great benefit in influencing the health of the mother and in preventing infections. The vital contribution of ascorbate to the body tissues can be summed up in the formation and maintenance of normal intercellular material, especially in the connective tissue, bones, teeth, and blood vessels. Genetic errors might be prevented if prospective mothers were advised to take 10 or more grams of ascorbate daily. It is significant that we found in the simple stress of pregnancy, a normal physiological process, that equivalent requirements paralleled those found in the rat when under stress. Experiments by King et al.[68] have shown that the need for supplemental vitamin C begins with the embryo.

Kidney Stones

The “scare” factor of large doses of ascorbate vs. kidney stones has been laid to rest. Since the urine is usually pH6, one can see that the opening of the lactone ring is a slow process. This reaction takes place in tissues and is probably regulated by the amount of glutathione present. The important considerations are that one must have a concentrated urine, that stasis must be a factor and that the urine must be alkaline for any appreciable amounts of the crystalloids to precipitate out. This will never occur with massive ascorbate therapy. Furthermore, it has been shown that the controls in a given experiment had almost as much oxalic acid spill as did those volunteers taking 9 grams of ascorbate daily.

Insect – Snake Bites

The quickness of results in snake bite, spider bite, hornet stings and caterpillar reactions demonstrates the usefulness in saving lives. It is best to give the vitamin intravenously with a syringe since bottle preparations are too time consuming. One precaution must be given. There exist a 2 gram ascorbate ampoule, and ironically it is the only one to my knowledge approved by the Food and Drug Administration, which might “kill” if used undiluted in a syringe. This lethal factor is due to the preservatives added. Each ampoule contains 2 grams sodium ascorbate. Vehicle contains: Monothioglycerol 0.14%; Sodium Formaldehyde Sulfoxylate 0.05%; Methyl Paraben 0.13%; Propyl Paraben 0.015%. Neutralized to pH6 with Sodium Bicarbonate; Water for injection q.s. This ampoule can be used intravenously ONLY when diluted to at least 25 c.c. to one gram. One sometimes will be confronted with extraordinary allergic and shock symptoms along with acute respiratory obstruction. In these situation one must employ Benadryl intravenously and/or intramuscularly and an adrenocortical hormone such as Decadron. These can be given by a nurse while the ascorbate is being prepared. In their absence a second “syringe” dose of ascorbate will suffice. Fluids by mouth should be given to prevent or correct thirst which all patients seem to experience.

Diabetes

Large doses of ascorbate do not cause diabetes mellitus in humans as has been suggested. On the contrary 10 grams daily, by mouth, has proved to be beneficial. The fact that 10 grams will allow them to heal wounds like normal individuals will save many legs in the future. Lamden, a biochemist, instigated these fears by misinterpretation of the results reported by Patterson using the Ketone formula intravenously in rats. [That is 100x the largest amount of ascorbate Klenner gave to humans, and a different form (see [above](#)).]

In Surgery

In surgery the use of ascorbate resolves itself into a “must” situation. The 24 hour frank scurvy levels should be sufficient evidence to encourage all surgeons to use vitamin C freely in their fluids. Proper employment of vitamin C by the surgeons will all but eliminate the post-surgery deaths.

In Malignancy

The part very large doses of ascorbate given intravenously over a prolonged period offers a medical challenge. From cabbage and tomatoes grown in the carbon-14 chambers radioactive ascorbate can be extracted, which can be used in tracer studies. At least one research team has demonstrated that in cancer all available “C” is mobilized at the site of the malignancy. Lauber and Rosenfeld reported that “C” is mobilized from the tissues of the body and selectively concentrated in traumatized areas. In one hopeless case we administered 17 grams daily for 92 consecutive days without changing the blood or urine levels from that associated with scurvy. This is the reason we believe a dose range of 100 grams to 300 grams daily by continuous intravenous drip for a period of several months might prove surprisingly profitable. Blood chemistry should be followed daily with such an investigation. Schlegel found that even a dose of 1.5 grams a day, by mouth, would prevent bladder cancer.

Barbiturate Poisoning

Our findings in no less than 15 cases of barbiturate poisoning suggested that no death should occur from this error in judgment. We also observed the dramatic effect of 12 grams intravenously on blood pressure associated with shock. The shock seen in heat stroke had been corrected by the time the injection was completed. The dose range used was 500 mg per Kg body weight.

Tetanus – Trichinosis

The use of ascorbate with Tolserol in the treatment of Tetanus should be accepted as universal treatment. Here again the dose must be proper. Our case as reported will serve as a guide in making these calculations. Ascorbate along with Para-Aminobenzoic acid is curative in Trichinosis. Both drugs are administered by mouth. It is estimated that at least 5 million cases of chronic Trichinosis exists in the United States. Just nine days of treatment would return these individuals to normal. In our cases 10 grams ascorbate was given daily and Para-Aminobenzoic acid was employed in high range. Four to six grams to start then three grams every 2 hours for eight times. For the remainder of the nine day schedule it was given 3 grams every two hours during the day and every three hours during the night.

Viral Hepatitis

Ascorbate is the drug of choice in viral hepatitis. The dose used ranges from 400 mg to 600 mg per Kg body weight, depending on the severity of the disease. It should be given every 8 to 12 hours. Ten grams ascorbate daily in divided doses is also given by mouth. Those under 10 years the usual schedule of at least one gram for each year of life.

Multiple Uses

We have reviewed many other pathological conditions in which ascorbate plays an important part in recovery. To these might be added

- **Cardiovascular Diseases**
- **Hypermenorrhea**

- **Peptic and Duodenal Ulcers**
- **Post-operative and Radiation Sickness**
- **Rheumatic Fever**
- **Scarlet Fever**
- **Poliomyelitis**
- **Acute and Chronic Pancreatitis**
- **Tularemia**
- **Whooping Cough**
- **Tuberculosis**

In one case of **scarlet fever** in which Penicillin and the Sulfa drugs were showing no improvement, fifty grams ascorbate given intravenously resulted in a dramatic drop in the fever curve to normal. Here the action of ascorbate was not only direct but also as a synergist. A similar situation was observed in a case of **lobar pneumonia**. In another case of **purperal sepsis** following a criminal abortion the initial dose of ascorbate was 1200 mg per Kg body weight and two subsequent injections were at the 600 mg level. Along with Penicillin and Sulfadiazine an admission temperature of 105.4°F was normal in nine hours. The patient made an uneventful recovery. In one spectacular case of **Black Widow**^[69] spider bite in a 3 1/2 year old child, in coma, one gram calcium gluconate and 4 grams of ascorbate was administered intravenously when first seen in the office. Four grams ascorbate was then given every six hours using a 20 c.c. syringe. She was awake and well in 24 hours. Physical examination showed a comatose child with a rigid abdomen. The area about the umbilicus was red and indurated, suggesting a strangulated hernia. With a 4 power lens, fang marks were in evidence. Thirty hours after starting the vitamin C therapy the child expelled a large amount of dark clotted blood. There was no other residual. A review of the literature confirmed that this individual has been **the only one to survive with such findings**; the others were reported at autopsy. Ten grams vitamin C and 200 mg to 400 mg vitamin B-6, by mouth, daily will **“shield” one from mosquito bites**. Twenty percent will also require 100 mg vitamin B-6 intramuscularly each week.

General Nutrition

Vitamin C plays a very important role in general nutrition. Deficiency of this substance in sufficient amounts can be a factor in **loss of appetite, loss of weight or failure to grow, muscular weakness, anemia** and various **skin lesions**. The relationship between vitamin C and the health of the **gums and teeth** has long been recognized. Laboratory studies on gum-teeth connective tissue have reaffirmed this relationship.^[70] Our son who will be 19 in July has **never developed a tooth cavity**. Since age 10 he has received at least 10 grams ascorbate, daily, by mouth. Before age 10 the amount given was on a sliding scale.^[71]

Intravenous Application

Ascorbate must be given by needle to bring about quick reversal of various “insults” to the human body. We have found that doses must range from 350 mg to 1200 mg per Kg body weight. Under 400 mg per Kg of body weight the injection can be made with a syringe provided the vitamin is buffered with sodium bicarbonate with Sodium Bisulfite added. Above 400 mg doses per Kg body weight, and a particular ampoule described in this summary, the vitamin must be diluted to at least 18 c.c. of 5 per cent dextrose in water, saline in water or Ringer’s solution. Many times Adenosine 5-Monophosphate, 25 mg in children and 50 to 100 mg in adults, given intramuscularly, is necessary to achieve results. The aqueous solution is more effective for quick results, although Adenosine in Gel can be employed. In debilitated individuals or when the pathology is serious, Desoxycorticosterone Acetate (DCA), aqueous solution, must also be added to the schedule. Usually 2.5 mg for children and 5 mg for adults is the daily intramuscular dose required. Sudden swelling of the feet indicates abnormal sensitivity and the drug must be discontinued.

It must be remembered when using ascorbate that experiments on man are the only experiments which can give positive evidence of therapeutic action in man. Likewise, the use of ascorbate in human pathology must follow the Law of Mass Action:

In reversible reactions, the extent of chemical change is proportional to the active masses of the interacting substance.

FRED R. KLENNER, M.D.

Reidsville, N.C.

Appendix

Case History: **Pesticide Poisoning**

Three boys ranging in years from age seven to age 12 were walking along a North Carolina Highway. They were caught in the "spray" of a dusting airplane. The youngest boy had been covered by the other two and so received little exposure. He was seen in the emergency room of the local hospital and sent home. The other two boys had different physicians. One lad age 12, under our care, was given 10 grams of ascorbate with a 50 c.c. syringe every 8 hours. The concentration was one gram for each 5 c.c. diluent. He was returned home on the second hospital day. The third boy received supportive treatment but did not receive ascorbate. His body was something to see. The spray had produced an allergic dermatitis as well as a chemical burn. He **died** on the 5th hospital day.

Case History: **Nasal Diphtheria**

Three children, living in the same neighborhood, developed nasal diphtheria. All three children had different physicians. A little girl under our care was given 10 grams ascorbate, intravenously, with a 50 c.c. syringe every 8 hours for the first 24 hours and then every 12 hours for two times. She was then put on one gram ascorbate every two hours by mouth. She lived and is now a graduate nurse. The other children did not receive ascorbate and both died. Our young patient also received 40,000 units diphtheria antitoxin which was given intraperitoneal. The other children also were administered the antitoxin.

Case History: **Poliomyelitis**

Although we were able to cure many cases of polio with massive doses of ascorbate, one single instance demonstrates the value of vitamin C. Two brothers were sick with poliomyelitis. These two boys were given 10 and 12 grams of ascorbate, according to weight, intravenously with a 50 c.c. syringe, every eight hours for 4 times and then every 12 hours for 4 times. They also were given one gram every two hours by mouth around the clock. They made complete recovery and both were athletic stars in high school and college. A third child, a neighbor, under the care of another physician received no ascorbate. This child also lived. The young lady is still wearing braces.

Case History: **Acute Virus Infection** representing **Deadly Virus Syndrome**

Cases with **paralysis** are extremely interesting in as much as they challenge diagnostic prowess. One of our cases, a female age 58, demonstrated three different types. She entered the hospital because of a convulsive seizure. She had had a **lingering cold** for ten days. She experienced three additional convulsive seizures after hospital admission. The temperature was 100.8°F pulse 140, respirations 32. She was extremely restless. Twenty-four grams ascorbate in 360 c.c. 5D water was given intravenously for three times at 8 hour intervals. One gram calcium gluconate was added to the first and third bottle. Twenty four hours following admission and 72 grams ascorbate in the blood stream, patient was awake and rational but

completely paralyzed, right arm and leg. Five grams ascorbate was given in fruit juice every 6 hours by mouth and 6 grams ascorbate along with a B complex preparation was given intravenously, daily for eight additional days. The right arm and leg returned to normal 48 hours after admission. Classical **pellagra** was also corrected during this hospital stay.

Case History: **Repeating virus infection**

This case proved that adequate ascorbate **therapy must be continued** long enough to destroy all virus bodies, otherwise the infection will recur. In 1960, I treated a seven year old boy, off and on, over a period of six weeks, for influenza like symptoms. Therapy included one of the mold derived drugs, sulfadiazine and 5 to 10 grams ascorbate by mouth. On three different occasions this treatment schedule was dramatically effective. When the child became ill for the fourth time, the administration of the above antibiotics and oral vitamin C had no reversing effect. On the third day of this illness the child suddenly became lethargic and just as suddenly to frank stupor. The temperature which had been running low grade was now 102.6°F. At this point all oral medication was discontinued. I immediately gave six grams of ascorbate intravenously with a 30 c.c. syringe. He was awake and asking, “what happened” in 5 minutes. Six grams ascorbate was given in 4 hours and then at 6 hour intervals for two additional doses. The recovery was complete in 24 hours and remained so. Ascorbate was again started by mouth giving 5 grams in juice every 8 hours. After one week, this was reduced to the usual daily “take” of seven grams. I had ample opportunity to observe this case—the child was our son.

Case History: **Snake bite**

Child of 4 years was struck on the lower leg by a large highland moccasin at 7:00 P.M., while at play in the yard of her country home. Seen in the emergency room of the local hospital at 7:30 P.M., the child was vomiting, was crying because of severe pain in her leg, which she held with both hands above the “fang marks”. Fever was 99.0°F. Four grams of ascorbate was given intravenously at 7:35 P.M. with a 20 c.c. syringe. The following 25 minutes were taken to follow a skin test on anti-venom. At this time and before the anti-venom was administered the child had stopped vomiting, she had stopped crying and was sitting on the emergency room table, laughing and drinking a glass of orange juice. She commented: “Come on, Daddy, I’m all right now, let’s go home.” She was allowed to return home with the understanding that her father would give me a report, by phone, each hour during the night. This he did. His report, each time, was that the child was sleeping as usual and that except for moderate swelling to the “calf of the leg”, appeared normal. Seen in the office at 10:00 A.M. the following morning she still demonstrated the small amount of swelling of her leg and had 1/2 degree fever. She was given a second dose of 4 grams of ascorbate intravenously. Seen at 5 P.M. she had no fever but the swelling remained constant. There was no pain. The following day, 38 hours after being bitten, she was completely normal. Since this was our first case of snake bite treated with vitamin C, we elected to give an additional 4 grams of ascorbate on this visit. No other antibiotics were given and none was required. Since she had had a booster injection of tetanus toxoid in recent months, none was given at this time.

Compare this to an earlier case of snake bite in a 16 year old girl, struck by a moccasin of about the same size, as gauged from the fang marks, on the hand while pulling tobacco plants, and who was hospitalized for three weeks. She was given 3 doses of anti-venom. The arm was compressed continuously with magnesium sulfate solution. Swelling was four times that of the opposite arm and striae developed over the entire surface. This patient received no vitamin C other than that found in a regular hospital diet. Morphine was required to control pain. (**We no longer use anti-venom.**)

Case History: **An Insidious virus**

This was a child of 18 months. She was seen in the driveway to my home at about 7:00 P.M. The history was brief. The child had strangled on food while eating supper. A cursory examination given in the front seat of an automobile revealed an extremely restless, whining child. The temperature was 98.6°F (axillary 10 minutes, corrected). There was no obstruction to the air-ways. We did elicit the information, that the

child had had a **cold for several days**. We also learned that the child's mother had taken her for a long stroller ride the previous day—which in this area was damp and cold. Frankly the impulse to send the child home was great.

Remembering that I had seen **children dead within 30 minutes to two hours** after hospital admission without treatment, I decided to buy some time. The Uncle was asked to take the child to the emergency room of the local hospital. The nurse on duty was given an order to take a rectal temperature and then give a fleets enema. If the results proved unsatisfactory, she was to repeat the procedure in 30 minutes using a normal saline solution. Approximately 45 minutes after leaving my home, the intern on duty reported by phone, that the child was unconscious to a point where she responded only to pain stimuli. The enema had not been given. Going at once to the hospital, conditions were found as described. The little patient was lying motionless on the examining table. Using a suitable size rectal tube I gave the enema with good results. The stool was normal. Rectal temperature taken at the hospital was 98.4°F (corrected). The pulse rate was 152 per minute and respirations were 32 per minute. It was impossible to visualize the throat because the mouth was “locked” as one finds after stimulation in lockjaw. Our impression was that the virus had now entered the brain.

Thirty grams of ascorbate, in divided doses, was given intramuscularly over a period of 36 hours. Crystalline penicillin was started on the second day and 300,000 units were administered in divided doses over the next three days. This was added to block secondary invaders. One hour following admission we applied a 4 x 4 gauze, saturated with tap water, to the child's lips. The sucking reflex was still intact, but the child immediately strangled. Turning the child head down, the small amount of water ran from its nostrils. Now it was clear. It was this “**bulbar phenomenon**” that was at play when the child was eating supper. The nursing log showed the temperature to be 99.0°F (corrected) 1 1/2 hours after admission and 1 1/2 hours later it was recorded at 100.0°F (corrected). The nursing log at this time read: “Shows no sign of consciousness.” Temperature was 101.2°F four hours after admission and was 102.4°F (corrected) after six hours. Now the nursing log read: “Baby swallowed water without difficulty.” At this point the temperature curve started back down and by 7:00 A.M. (11 hours following admission) the child was alert and taking water freely from a spoon. Twenty eight hours after the first injection of ascorbate the temperature was normal. Water, milk and orange juice were now taken from a bottle. Cecon (liquid vitamin C) was given by mouth. Discharge was on the 5th hospital day. The **initial low fever recording indicated that the child was dying**; after ascorbate therapy she began to respond, thus the fever. After the virus was killed, the temperature returned to normal.

Case History: **Monoxide Poisoning**

State highway employee carried into my office in unconscious condition. He was a known diabetic. The breathing was not Kussmaul type and his skin was warm and dry. We elicited the information that he had been found in the cab of his truck with the windows closed and the engine running. It was a cold Winter day. Entertaining a diagnosis of Monoxide intoxication we immediately gave 12 grams ascorbate with a 50 c.c. syringe using a 20 gauge needle. (We employ a 20 G. needle when using a 50 c.c. syringe; 21 G needle for a 30 c.c. syringe; 22 G needle for a 20 c.c. syringe and a 23 G needle for a 10 c.c. syringe. This assists in controlling the rate of flow which is important, especially, in young children). Within 10 minutes the patient was awake, sitting up on the edge of the examining table, rubbing his eyes and saying: “Doc, what in the world am I doing up here in your office.” He returned to his place of employment within 45 minutes.

Case History #1: **Acute Virus Pancarditis**

A five year old boy was admitted to the local hospital with history of having a “relapse” after recovery from **measles**. The physical findings showed a thready and feeble pulse. A distinct rub was in evidence by auscultation. The EKG showed RS-T deviations. The temperature was 105°F. Ascorbate calculated at 400 mg per Kg body weight was given intravenously with a syringe. Within two hours the picture had almost reverted to normal. Injection of Vitamin C was repeated in 6 hours and again at 12 hours. A fourth injection

was given after 24 hours although the patient was clinically well. The child returned home on the 4th hospital day.

Case History #2: **Acute Virus Pancarditis following a deep cold**

The findings approximated those of case #1. The parents elected to take the child to Duke Medical Center. Six grams of ascorbate was given by needle before starting the trip to the hospital which was 60 miles away. Upon arrival at the Medical Center the child had made such dramatic response to the single injection of ascorbate that the parents were tempted to return home. The receiving physician questioned the sickness of the child as being out of proportion to that relayed by me during our telephone conversation. The parents assured the physician that the child had been seriously ill, but that the change came about after receiving the ascorbate. Although 50 grams (25 ampoules) of ascorbate was sent along with the parents, none was given because the physician in charge stated that he would be afraid to give that size dose, intravenously, to a child. The fact that we had administered six grams, which represented a dose of 400 mg per Kg body weight, apparently had no influence. Laboratory findings, however, confirmed our impression and the child was hospitalized for two weeks. Two additional injections of vitamin C would have cured the child in 24 hours.

Case History: **Acute Pancreatitis**

Adult Male seen in the emergency room of local hospital complaining of severe, agonizing pain in the epigastrium which radiated to the back. Nausea and vomiting were present. Serum amylase studies showed a concentration of 345. This was the 4th such attack experienced by this patient. Sixty grams ascorbate in 700 c.c. Dextrose in water was given intravenously. 20 mg Pantapone was given in the emergency room. No additional opiates were required. The patient made an uneventful recovery. He was placed on 10 grams ascorbate by mouth and has not had a recurrence in almost 5 years. He has, however, developed mild diabetes mellitus which is now controlled with diet and vitamin C.

END

I am in full agreement with Lancelot Hogben who said, "A scientific idea must live dangerously or die of inanition. Science thrives on daring generalizations. There is nothing particularly scientific about excessive caution. Cautious explorers do not cross the Atlantic of truth."

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Frederick R. Klenner, M.D., F.C.C.P. (1907-1984)

Reidsville, North Carolina

A native of Pennsylvania, Dr. Klenner attended **St. Vincent and St. Francis College**, where he received his **B.S.** and **M.S.** degrees in biology. He graduated **magna cum laude** and was awarded a teaching fellowship there. He was also awarded the college **medal** for scholastic philosophy. There followed another teaching fellowship in chemistry at **Catholic University**, where he pursued studies for a doctorate in physiology.

Dr. Klenner then ‘migrated’ to North Carolina and Duke University to continue his studies. He arrived in time to use his knowledge in physiology and chemistry to free the nervous system of the frog for a symposium by immersing the animal in 10% nitric acid. Taken in tow by Dr. Pearse, chairman of the department, he was finally persuaded to enter the school of medicine. He completed his studies at Duke University and received his **medical degree in 1936**.

Dr. Klenner served three years in post graduate hospital training before embarking on a private practice in medicine. Although specializing in diseases of the chest, he continued to do general practice because of the opportunities it afforded for observations in medicine. His patients were as enthusiastic as he in playing guinea pigs to study the action of ascorbate. The first massive doses of ascorbate he gave to himself. Each time something new appeared on the horizon he took the same amount of ascorbate to study its effects so as to come up with the answers.

Dr. Klenner's list of honors and professional society affiliations is tremendous. He is listed in a flock of various "Who's Who" registers. He has published many scientific papers throughout his scientific career.

Eight Decades of Scurvy. The Case History of a Misleading Dietary Hypothesis.

Irwin Stone. PC-A¹

This paper will discuss the history of scurvy in this country over the past eight decades and try to explain how a potentially-fatal and insidious genetic disease of such wide incidence in our population could become an unrecognized, phantom disease, to which most present day doctors pay little or no attention and are unconcerned. It will also discuss the widely accepted dietary theory which has been applied by nutritionists attempting to solve this problem in medical genetics. The author believes that the wide acceptance of this misleading dietary hypothesis is the source of the medical complacency and apathy and the dangerous continuing high incidence of Chronic Subclinical Scurvy.

Scurvy is a disease which during the course of human prehistory and recorded history has killed more victims, caused more disease and suffering and has shortened the human life span more than any other single factor. (Stone, 1972). This disease has been epidemic among humans ever since they appeared on this earth. If it weren't for the high mortality of scurvy and its efficient control

Hyannis, Massachusetts, July 16, 1978 and also presented at the Annual Meeting of the Orthomolecular Medical Society, September 17, 1978, San Diego, California.

of population growth, our problems of overpopulation would have overwhelmed us centuries ago.

Many people believe that scurvy is not a modern disease because they think the problem was solved in the 18th Century when Dr. James Lind of Britain's Royal Navy (Lind, 1753) found that one ounce of fresh lemon juice would prevent the appearance of the terminal symptoms of this dread disease in his scorbutic sailors.

Others, including nutritionists, home economists and a large proportion of the medical profession believe that the minute daily doses of "Vitamin C" proposed in 1912 in the "Vitamin C-Dietary Deficiency Disease Hypothesis" (Funk, 1912) has completely solved the problem of scurvy and there is nothing further to worry about. Nothing could be further from the truth.

Let us take a look at the sequence of historical events in scurvy of the past 80 years and try to see what went wrong and what finally went right:

The first notable date in this century is 1907 which records the first important scientific advance in our knowledge of scurvy beyond what was known to Dr. Lind in 1753. Hoist and Frohlich (1907) stumbled accidentally upon this important evidence while they were investigating ship beriberi which was causing problems in the

¹ 1331 Charmwood Square, San Jose, California 95117

This paper was originally prepared for presentation at the Conference On Controversies In Human And Clinical Nutrition, Boston University School of Medicine,

Norwegian Fishing Fleet.

Up until 1907, scurvy was considered to be solely a human disease because none of the animals used in medical experimentation up to that time, appeared susceptible to this disease. No matter how deficient a scorbutic diet was fed laboratory rats or mice, none ever died of scurvy. In ship beriberi the standard test animal in 1907 was the pigeon. Hoist and Frohlich wanted to use a small mammal instead of a bird so they tested guinea pigs by feeding them a diet that caused beriberi in pigeons. To their amazement they found that the guinea pigs developed scurvy instead. We now know why this is so, but in 1907 it was a complete mystery. Guinea pigs suffer from the same genetic defect as humans. The result of Hoist and Frohlich's work was to provide a small test animal that could be used in laboratory experiments on scurvy. Later, monkeys were also found to be susceptible to scurvy. Guinea pigs or monkeys are the only test animals that should be used in any medical experiments where results are to be extrapolated to humans. Rats, mice, rabbits, dogs and all other animals capable of synthesizing ascorbate endogenously are unsuitable as test animals in this medical experimentation.

The second date is 1908. This is a date that is not usually connected with the history of scurvy, but 57 years later in 1965, the work reported in 1908 supplied the clue which placed scurvy into its rightful place as an inherited illness, a potentially-fatal genetic liver-enzyme disease. It was in 1908 that Sir Archibald Garrod, a noted English physician, who was at least 50 years ahead of his time, published his series of Croonian lectures describing a new type of disease, an "inborn error of metabolism" which is caused by a missing or a defective, inactive enzyme. As is usual with great medical discoveries, Sir Archibald's exciting concept and clinical results were ignored for forty years before being "rediscovered" in the 1950's. Now there are thousands of "missing enzyme" diseases, including "Hypoascorbemia", the actual cause of scurvy.

Four years later in 1912, nutritionists led by the Polish biochemist, Casimir Funk summarized the

nutritional knowledge of the 19th Century and early 20th Century and came up with the revolutionary idea that these diseases could be caused by the lack of some trace substance in the diet. They cited three diseases as typical of these deficiency diseases: xerophthalmia, an eye disease, beriberi, a deadly neurological disease of the Far East, and the third one -scurvy. The unknown, hypothetical missing substances in the diet causing these diseases were named "vitamines" A, B and C respectively for each of these diseases. This "vitamin" hypothesis appeared to be a perfectly logical explanation of the state of the nutritional knowledge available in 1912. Later research on these diseases has shown that the results on the diseases caused by the lack of vitamin A and the B vitamins have stood the test of time better than scurvy and vitamin C.

Any hypothesis is only as good as the confirming later research and a theory has to be revised periodically in the light of this continuing research. The research of the past 15 years has exposed serious flaws in the vitamin C-Dietary Deficiency Disease

Hypothesis for the etiology of scurvy and broad revisions are required in this hypothesis to bring it in line with the current facts.

In 1912, the antiscorbutic factor was arbitrarily named vitamin C and its existence was neither proven or even known to exist at the time. There were many other theories prevalent at this time, such as that scurvy was caused by tainted meat or by constipation, so in 1912 this was a very tenuous hypothesis. It took twenty years and much intensive chemical and biological research before it was proven in 1932 that the hypothetical antiscorbutic substance, "Vitamin C" was actually ascorbic acid.

At that time the chemical structure of ascorbic acid was worked out and its synthesis was devised and for the first time in the history of mankind, ascorbate, the specific antidote for scurvy was available in unlimited quantities as the pure unadulterated crystalline product.

Before this, large quantities of fresh foods had to be used to provide precious little of this wonder substance. The potato, for

instance, which was the main antiscorbutic foodstuff of the entire population of countries like Ireland in the 19th Century, requires the ingestion of at least 44 pounds of boiled potatoes to obtain a level teaspoonful of ascorbic acid (3 grams). So you see that in the early days before the synthesis of ascorbate everyone was thinking in terms of minute food related dosages. This is why the early workers became misorient-ed in the direction of minute inadequate daily intakes of vitamin C. They could not use more because they were always limited to foodstuffs containing only minute quantities of vitamin C. Then when pure ascorbic acid suddenly became available, they could not change this enforced pattern of thinking and continued to look into smaller and smaller daily doses.

As a consequence, the nutritionists and home economists who dominated the research effort at that time, conducted test after test to find the smallest amount of vitamin C which would prevent the appearance of the Classical Terminal Signs of Frank Clinical Scurvy and still avoid death, the so-called "Minimal Daily Requirements". However, in their entire research effort since 1912 they have never conducted a single, long-term test to determine the optimal level of the daily intake of vitamin C, the amounts of daily ascorbate intake that are needed for full health and to maintain this health and freedom from disease throughout a person's lifetime. This record of research shortsightedness by the nutritionists over the past 66 years is only paralleled by the lack of hard data for setting the current Recommended Dietary Allowances (RDA) for ascorbate to maintain the full health and freedom from disease of the American people. The present adult RDA for ascorbate is not based on any tests or clinical data but is just a collection of guesses and assumptions. The Food and Nutrition Board that sets the official RDA's has been steadily reducing the RDA for ascorbate with each new edition of its book in face of the mounting evidence that more and more ascorbate is needed to combat the present increasing stresses of living. The present RDA's for ascorbate is at least 300

times less per unit body weight than the amount of ascorbate produced endogenously each day by other mammals to maintain their own bodies in a good healthy condition and fight off their stresses. This is a discrepancy that I've never seen adequately explained by the current low-ascorbate-dosage enthusiasts.

Several other grave errors have been made with this hypothesis from the early days. The classical signs of scurvy are used as a means of diagnosing "scurvy". These classical symptoms are really the terminal sequelae of Frank Clinical Scurvy and this theory ignores and bypasses the relatively asymptomatic, insidious Chronic Subclinical Scurvy which is epidemic in our population. Another early grave error was equating good health with the mere lack of these terminal symptoms. The present RDA of 45 mg will prevent the appearance of these terminal symptoms but it won't do much for correcting the Chronic Subclinical Scurvy. This is like saying cancer victims are in good health as long as the terminal signs of the disease are not evident.

Biochemical research in the 1950's showed that the lesion in scurvy is the absence of the enzyme, L-Gulonolactone oxidase (GLO) in the human liver (Burns, 1959). This enzyme is the last enzyme in a series of four which converts blood sugar, glucose, into ascorbate in the mammalian liver. This liver metabolite, ascorbate, is produced in an unstressed goat for instance, at the rate of about 13,000 mg per day per 150 pounds body weight (Chatterjee, 1973). A mammalian feedback mechanism increases this daily ascorbate production many fold under stress (Subramanian et al., 1973).

The lack of the enzyme GLO in the human liver completely blocks the endogenous biochemical synthesis of ascorbate and has destroyed the ability of humans to produce their own ascorbate. There are a few other mammals afflicted with this same genetic defect as humans, such as, guinea pigs and other members of the Primate Sub Order, Anthropoidea. Complete deprivation of ascorbate is rapidly fatal. It takes several months for humans to die from scurvy

depending upon the incident stresses, but a guinea pig succumbs in two weeks. Scurvy, therefore, meets all the criteria of the genetic diseases, the "inborn errors of metabolism" the "missing enzyme" diseases described by Sir Archibald Garrod in 1908.

In 1956-67, in a series of four papers (Stone, 1965) it was shown that scurvy was not a separate dietary disease entity but merely the premortal sequelae of a genetic liver-enzyme disease, Hypoascorbemia. Thus instead of being a simple dietary disturbance due to the lack of vitamin C in foods, the basic cause of our susceptibility to scurvy is the much more serious potentially-fatal inherited presence of a defective gene for GLO in the human gene pool. This defective gene appears to have originated by a mutation in a primitive primate ancestor of Man, some 60 million years ago (Stone, 1972) and its incidence is in 100 per cent of the human population.

We now have the paradoxical situation of a basically inaccurate hypothesis dominating the thoughts and research for over 60 years in a field where no attempts have been made during this time to bring this theory into line with established facts. It has been a record of a serious potentially-fatal genetic liver-enzyme disease, an "inborn error of carbohydrate metabolism" being investigated by nutritionists and home economists, under the mistaken impression that it is a simple dietary disorder. Such little progress in improving human health in the past 80 years of clinical research can be attributed to the narrow outlook and low dosage orientation of the investigators due to the fact that they were neither qualified by training or competent by experience to be investigating a complicated problem in medical genetics. The most serious result of this long exposure to misleading nutritional propaganda is that this hypothesis has become current medical dogma and has prevented the easy and simple elimination of Chronic Subclinical Scurvy (the CSS Syndrome) in our population and has permitted this disease to reach epidemic proportions (Stone, 1977).

Because of this misleading hypothesis, the current impression in the minds of a large

segment of physicians is that 1. scurvy is a rare disease in this country; 2. that if you take 45 mg of ascorbate a day scurvy is "cured" and there is nothing further to worry about; 3. the only disease that ascorbate (or "vitamin C") can treat is scurvy; 4. doses of 150 mg of ascorbate a day for a human adult are not only unnecessarily high, but may be toxic and are "wasteful".

The clinical research of the past decade has shown these impressions to be sheer nonsense. 1. Chronic Subclinical Scurvy (the CSS Syndrome) is our most widespread disease (Stone, 1972). 2. 45 mg of ascorbate will prevent the appearance of the terminal symptoms of the disease but will not do much else. To correct Chronic Subclinical Scurvy requires at least 10 grams of ascorbate a day depending upon the incident stresses (Stone, 1977). Under heavy stresses the daily ascorbate requirement may be 200 grams or 300 grams to keep ahead of the CSS Syndrome. 3. The long term biochemical results of Chronic Subclinical Scurvy set the stage for the development of the serious medical problems of later life; the heart attacks, the cancer, the collagen diseases and many more. Preliminary clinical tests indicate that mega levels of ascorbate are useful in the prevention and treatment of cancer (Stone, 1974, 1976), heart disease, and many others (Stone, 1972). In the case of viral diseases (Pauling, 1978, Stone, 1972), research of the past 30 years indicates that no one should succumb to a viral infection any more. Ascorbate is a non-specific, nontoxic virucide and when used at the proper daily dosage (up to 300 grams intravenously and/or orally) any viral infection can be relieved within 96 hours (Klenner, 1974, Cathcart, 1978, Pauling, 1976). The Sudden Infant Death Syndrome (SIDS) or Crib Death, has been shown by the Australian workers, A. Kalokerinos and G. Dettman, to be a manifestation of infantile scurvy, due to the fact that all infants, born of mothers who depended solely on their diet as their only source of ascorbate, are born with the CSS Syndrome after nine months of intrauterine scurvy (Stone, 1978). SIDS can be prevented by increasing the infant's intake of ascorbate (Cook, 1978). This has been known and

published since 1974 (Kalokerinos, 1974). Yet 8000 to 10,000 babies die of SIDS a year because the doctors and others involved with the management of these babies permit this annual slaughter to take place because they have become so complacent with scurvy that they refuse to even try this harmless treatment. 4. Ascorbate is one of the least toxic substances known. Therapeutic doses up to 300 grams can be administered without unfavorable side reactions. The daily doses that we recommend for humans are based on amounts normally synthesized by the mammals and should not be regarded as "high" or "abnormal" amounts. We are using the "normal" mammalian levels. It is the "micro" daily amounts recommended under the "Vitamin C-Dietary Deficiency Disease" theory that are the inadequate abnormally low levels.

Over the past 8 decades the use of these "micro" daily levels of ascorbate intake, much below the levels needed to overcome our current daily stresses of living, has served to wipe out acute Frank Clinical Scurvy as a common disease but has preserved the epidemic incidence of the CSS Syndrome, the more insidious and more dangerous, relatively asymptomatic form of scurvy. The full correction of the CSS Syndrome is the first step in any Preventative Medicine procedure.

As soon as the term "Vitamin C" is discarded in favor of "Ascorbate" when speaking of this missing Human Liver Metabolite, we shall know that some progress has been made in understanding this killer disease.

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Fifty Years of Research on Ascorbate and the Genetics of Scurvy: From a Better Flavored Beer To Homo Sapiens Ascorbicus Irwin Stone, D.Sc.

One thing certain in any long-term research program is that no matter where you start, you have no idea how it will end. In 1934, as head of a newly formed commercial enzyme and fermentation research laboratory, I had the opportunity to investigate the problem in industrial technology of improving the flavor stability of packaged beer. The problem was successfully solved by using the unique chemical properties of a new substance discovered and described only two years earlier by Albert Szent-Gyorgyi, M.D., Ph.D., — Ascorbic Acid. I went on to be awarded the first United States Patents on industrial uses of ascorbic acid in 1939, while Albert Szent-Gyorgyi received the Nobel Prize in Medicine in 1937 for his discoveries. I had not the slightest inkling at that time, that thirty-one years later in 1965 I would be describing a hitherto unrecognized human birth defect due to the presence of a mutated defective gene in the human gene pool.

If anyone asks me the embarrassing question, "What took you so long?", my answer is the lack of proper funding for my medical work. My industrial sponsors were not interested in the genetics of scurvy, and what do you do when you are two centuries ahead of the medical grant peer reviewers who hold

the purse strings? I did the best I could on my own time using my own meager funds.

In the period 1934 to 1965, one research idea led to another and many biochemical industrial and enzymatic problems were solved, resulting in about sixty technical publications and a score of U.S. Patents.

I early became aware, from my library research on the medical aspects of ascorbic acid that the recommended low daily intakes, the so-called "RDA's", of the multifunctional ascorbate-ion, which most everyone succumbing to the misleading 1912 nutritional propaganda regarded as the trace food substance, "vitamin C", seemed far below what a chemist would expect to be required for optimum reaction rates for a wide variety of vital biochemical functions in a 70 kg human. Besides, I searched the literature of the nutritionists, who with the unlimited financial backing of the food industry, had dominated the field of scurvy research in the 20th century. I could not find

This is the paper Irwin Stone was to present at the annual symposium of the Academy of Orthomolecular Psychiatry in Los Angeles in May. His sudden and untimely death occurred soon after he arrived at the conference. Tributes to Dr. Stone and to his colleague, Dr. Klenner appear on page 285.

a single paper that reported a properly designed, long-term double blind test to determine the optimum daily human requirements for ascorbic acid in health and disease and under a variety of stresses. Even now, over forty years after commercial pure ascorbic acid became available, nutritionists have not supplied us with this vitally important critical data. Instead, they have become so locked-in to their antiquated 1912 nutritional hypothesis, that they assume that scurvy can only be cured by dietary means by consuming a "normal" diet with plenty of fresh fruits and vegetables. The actual levels of ascorbate in foodstuffs are so low that when they calculated the adult RDA's they arrived at figures varying from 45 to 75 milligrams of ascorbate (vitamin C) a day, for the past several decades. This minuscule daily RDA is published, with a new edition every five years, by the National Academy of Sciences in Washington, D.C. in the publication entitled "Recommended Dietary Allowances", which has a semi-official status and is the bible for the nutritionists and the Food and Drug Administration. The latest edition gives the adult RDA for ascorbic acid as 60 milligrams a day, which they claim includes a "factor of safety". For overcoming the stresses of pregnancy, they recommend adding another 20 milligram intake for the pregnant female. More about this later when we discuss the Sudden Infant Death Syndrome.

Two M.D.'s who early and independently recognized the physiological inadequacy of these minuscule daily ascorbic acid intakes were the scholarly Canadian physician, William J. McCormick, M.D., who had been practicing medicine since 1904, and the Megascorbic Medical Pioneer, the Reidsville North Carolina, "country doctor", Frederick R. Klenner, M.D. Dr. Klenner saved his own daughter from death and paralysis in the 1947 polio epidemic with mega doses of ascorbate. Both these great physicians published their views and case histories widely and I had the good fortune to meet both of them. While their innovative views fell upon the deaf ears of orthodox medicine and were completely ignored, they made a lasting impression on me and were a great factor in my continuing to work in this strange and frustrating field of orthodox medicine,

where the bulk of the practitioners seemed to have no desire to learn anything new and innovative, especially from a non-M.D. chemist.

Since the 1930's, when ascorbic acid first became commercially available, I and my family became our own guinea pigs, experimenting with the effect of these mega doses on our health and well being. As the prices of the ascorbate dropped our daily intake rose. I also early developed a megascorbic procedure for aborting the common cold, which in my tests was more than 95 percent effective. I haven't had a cold in over forty years. Starting about the mid-1940's, I had my laboratory repackaged ascorbic acid and sodium ascorbate in four ounce bottles which we sold to our fellow employees at cost. I noticed a drop in absenteeism due to sickness, and when they were on the job they seemed to have more stamina, were less tired and seemed to be smarter than their scorbutic counterparts.

In May, 1960, at a meeting in Minneapolis, I was elected Vice President of the American Society of Brewing Chemists, an organization in which I had long been active. This meant that I would become President in 1962-1963. After the meeting we decided to vacation in the Black Hills of South Dakota and see Mount Rushmore, but we never got there. Outside of Rapid City, South Dakota, we had a very serious automobile accident when a drunk driving on the wrong side of the road drove her car at 80 miles an hour into a head-on collision with ours. Both my wife and I were seriously injured and the only reason we survived was the fact that we had been regularly taking daily megadoses of ascorbate for decades. We never went into the deep shock that kills most accident victims and I was able to experimentally verify ascorbate's great healing power and survival value by taking about fifty to sixty grams a day of ascorbate during our hospitalization. My wife recovered quickly and acted as my "nurse". I went through five serious operations without any surgical shock and my multiple bone injuries healed so fast that we were able to leave the hospital in less than three months; take a 2,000 mile train trip home and I was back at work running my lab in two months more. I left the hospital, under my own steam, on crutches, walking on legs that the doctors originally

predicted I would not be able to stand on for at least a year. My larynx was damaged by part of the steering wheel inflicting a deep throat wound, and the doctors despaired that I would ever talk again. With the help of megascorbics, this problem slowly resolved and I was able to assume the public speaking duties of the President of a Scientific Society with a voice of a slightly different timbre. If you ask my wife, she will tell you that I now talk too much!

Most important, this accident impressed on me the need for immediate publication of the medical data on Megascorbics and the genetics of scurvy that I had been collecting for years. Originally I had planned to publish my medical ideas after I would be mandatorily retired at age 65 from my industrial connections.

The first four papers describing the genetics of scurvy and the human "inborn error of carbohydrate metabolism", *Hypoascorbemia*, appeared in the period 1965-1967. Hypoascorbemia is a potentially-fatal genetic liver-enzyme disease, a human birth defect caused by a defective gene in the human gene pool for the synthesis of the active enzyme protein, L-gulonolactone oxidase (GLO). This defective gene appears to be present in 100 percent of the human population and is the biochemical reason that the human liver is unable to complete the normal stress-related mammalian biochemical conversion of blood sugar, glucose, into ascorbic acid.

This is an extremely vital biochemical pathway that proceeds normally and continuously throughout the lifetime of the non-Primate mammals carrying the intact gene for GLO, producing large stress-related daily amounts of ascorbate in the liver, which is funnelled directly into the blood stream to give the necessary high blood and tissue levels of ascorbate required for the maintenance of biochemical homeostasis throughout the body.

Mammals with the intact gene for GLO also have an inherited biochemical feedback mechanism that increases the liver synthesis of ascorbate in response to various stresses. This feedback mechanism was a great factor in assuring the survival and dominance of the Earth by the mammals during the past 165 million years of evolution. Some of my later papers

indicate that a large group of mammals became extinct during this evolution because they could not make enough daily ascorbate for survival. Homo sapiens have paid a very high cost in deaths, disease and misery during the past few million years of evolution in trying to survive without the benefit of the intact gene for GLO. I regard Homo as our most endangered mammal, scheduled for extinction in the 21st Century from overpopulation pollution, unless humans take evolutionary destiny into their own hands and convert themselves into the robust human subspecies, Homo Sapiens Ascorbicus. Read my papers on "Homo Sapiens Ascorbicus"; I've published several since 1979.

I would like to show you at this point an exhibit of three test tubes. The first tube contains the amount of ascorbic acid that a 70 kg human produces in its liver each day. It is an empty tube. The second tube is over half full of ascorbic acid, which is the 13,000 mg that an unstressed 70 kg goat produces in its liver each day. Under stress the test tube would not be large enough to hold all the ascorbate produced. The small third tube contains the current RDA for ascorbic acid — 60 milligrams, barely enough to cover the bottom of the tube. This is the daily intake for 70 kg human adults recommended by nutritionists, physicians and the Food and Nutrition Board of the National Academy of Sciences in Washington, D.C. My recommendations for the daily intake of ascorbate would be close to the amounts synthesized daily by the mammals with the intact gene for GLO. In times of stress the intakes are increased and the extent of increase can be estimated by the bowel tolerance procedure of Dr. Robert Cathcart. I have been taking about 20 grams of ascorbate a day for many years which is over three hundred times the current RDA, enjoying full health during this time. In my 1983 paper on the effect of megascorbate on Aging and Alzheimer's disease, I cite as shining examples of the value of this daily megascorbic regimen in maintaining a long healthy active, disease-free life: they are my long time friends and colleagues, Albert Szent-Gyorgyi, 91; Linus Pauling, 83; Frederick Klenner, 77; and myself, 77; all still working hard and none showing the slightest

trace of Alzheimer's.

I regard as one of the major blunders of 20th Century medicine the full acceptance of these inaccurate RDA's without conducting long-term double blind studies on their accuracy and effectiveness in health and disease. This blunder is further compounded by the medical schools teaching these antiquated ideas on scurvy to our future doctors, two decades after I showed that scurvy was a deadly problem in medical genetics. For the first time in millions of years, it was possible in the early 1940's to "cure" scurvy when inexpensive pure ascorbic acid became commercially available. Medicine did nothing at this time because there was no one around at that time with sufficiently accurate knowledge of the genetics of scurvy to guide them. This excuse was eliminated with the publication of my 1965-67 papers on the genetics of scurvy, but they still took no steps to fully correct this human birth defect, and eliminate the health threatening effects of this widespread iatrogenic epidemic of Chronic Subclinical Scurvy.

Except for medical friends, colleagues and many sick non-medical lay persons, the bulk of the medical establishment ignored this work and to them it was "business as usual." They never gave themselves the opportunity to observe the improved therapeutic results they would obtain when their sick patients were free of the debilitating lifelong Chronic Subclinical Scurvy.

In the 1960's I interested Dr. Linus Pauling in my early work and my technique for aborting the common cold. He confirmed my work and his life has never been the same since. This led to the publication of his 1970 book, *Vitamin C and the Common Cold*, which in later editions became *Vitamin C, The Common Cold and The Flu*. In 1979, *Cancer and Vitamin C*, appeared which described his cancer collaboration with Dr. Ewan Cameron.

I started publication of my megascorbic leukemia ideas in 1974. In 1975, as a result of my collaboration with my good friend, Wendell O. Belfield, D.V.M., we wrote a paper showing the need for and the good results obtained with megascorbic therapy in cats and dogs, even though they had the intact gene for GLO. We found that cats and dogs were poor producers of daily ascorbate in their livers. They made about

one-fifth the daily amount produced in other mammals with the intact gene for GLO. For many years, Wendell had been independently using Megascorbics with great success in canine distemper (viral encephalitis) and in hip dysplasia in large dogs. He also recently megascorbically solved the problem of cat leukemia, the number one killer of pet cats. He, like his counterparts in human medicine, has had his problems with the veterinary medical establishment. His two books on dogs (1981) and cats (1983) are classics in maintaining these pets in good health.

My cancer suggestions were published in 1974, 1976, 1977 and 1981. In my 1983 paper, presented at the Orthomolecular Medical Society meeting in San Francisco, I reported on the remarkable case of Joseph Kieninger, chemist and patent attorney, terminal cancer victim turned successful therapist. Joe is a prostatic cancer victim, whose cancer has spread throughout his body. He was declared terminal in 1977 and given about one year to live. By his innovative daily treatments both systemic (beginning with 80 to 100 grams sodium ascorbate a day, every day) and topical megascorbic applications, he has survived to the present, living a pain-free, relatively normal life, going to work each day and feeling good most of the time. I believe Joe is a prototype for survival in terminal disease and has shown us a new way of handling these highly scorbutic patients that Medicine has given up, and prevent them from dying of scurvy. Joe, a keen observer, wrote up and submitted his case history to the *New England Journal of Medicine*, but they returned his manuscript and refused publication. If I am correct in thinking of Joe as a terminal disease prototype, then this would put a different complexion on the Hospice Movement. Instead of terminal patients going to a hospice to die in dignity, they would go to be taught the inexpensive megascorbate regimen on how to *live* in dignity, and then go home and practice this regime for the rest of their lives.

No discussion of cancer would be complete without mention of my friend and colleague, Henry L. Newbold, M.D., of New York City, who in 1979 published his book *Vitamin C Against Cancer* (Stein and Day,

New York). It is now in an inexpensive paperback edition and should be read by every cancer victim as a "second opinion"; it may be life saving.

In 1973 I became acquainted with the work of Archie Kalokerinos, M.D. and Glen Dettman, Ph.D., of Australia on their mega-scorbic solution of the Sudden Infant Death Syndrome (SIDS). SIDS was also solved earlier in a similar manner by Dr. Klenner. My work indicates that because of the poor correction of the birth defect for GLO, every baby is born after a nine month bout with intrauterine scurvy. The first result of this is the Sudden Infant Death Syndrome. Klenner and Kalokerinos found that by increasing the daily intake of ascorbate by the pregnant mother (15 grams/day) and the neonate (100 mg/day) that SIDS could be eliminated. Publication of this simple, harmless procedure in the Australian medical literature brought down the wrath of the Australian medical establishment on these investigators. They refused to test Kalokerinos' procedure and allowed babies to die needlessly, because there is no other effective treatment for SIDS. I thought that this would never happen in American Medicine, but I was wrong and it is

happening here right now. The orthodox medical establishment is the same the world over. About 10,000 babies die each year in the U.S. from SIDS. To stem this slaughter, Drs. Kalokerinos and Dettman have come to the U.S. on biannual nationwide lecture tours since 1976, and they will be returning again in September 1984. Ten years ago Dr. Kalokerinos' book, *Every Second Child*, appeared in Australia. 1981 saw the publication of an American paperback edition (Keats Pub. Co. New Canaan, CT 06840). Since the publication of their book in 1974, 100,000 babies have died, sacrificed to medical bias and professional stubbornness and callousness. It is unbelievable.

This really is nothing new to me because I have constantly come up against similar hostility from the Medical Establishment when I tried to have clinical trials conducted after publication of my papers on leukemia (1974), veterinary medicine (1975), smoking (1976), cancer (1976), drug addiction (1977), sudden death (1978), endogenous interferon treatment of cancer and the viral diseases (1979-1981), multiple sclerosis (1982), aging and Alzheimer's disease (1983) and AIDS (1983).

In Memoriam

Irwin Stone 1907 -1984

Irwin Stone, a truly great pioneer in the field of vitamin C research, died on May 4, 1984, at the age of 77. Irwin was in Los Angeles to receive an award from the Academy of Orthomolecular Psychiatry and the Orthomolecular Medical Society. He was also to have received a surprise award from the Linus Pauling Institute of Science and Medicine. The death was accidental, caused by choking on regurgitated food. As the result of a near-fatal auto accident in 1960, in which severe throat injuries were sustained, Irwin suffered from a constricted esophagus, which made choking on food an ever-present danger.

Irwin Stone began his study of vitamin C, which he referred to as ascorbate, in 1932, as a chemist for the Wallerstein Company in New York. He was interested in the antioxidant properties of ascorbic acid, then newly discovered, as a means of protecting food against deterioration. He continued his study of vitamin C for the next 50 years, thereby making an immense contribution to the welfare of mankind.

Stone applied for three patents for the industrial use of vitamin C, in 1935, the first in history. Albert Szent-Gyorgyi received the Nobel Prize in medicine for his work on vitamin C only two years later, in 1937. Stone received a total of 26 patents, for his work in vitamin C as well as in other fields.

In the 1950s it became clear to Stone that humans would benefit from ingesting much larger amounts of ascorbates than the medical and nutritional establishments considered adequate. After he retired from his paid employment and moved to San Jose in 1971, he devoted the rest of his life to studying and publicizing the need for multi-gram daily consumption of vitamin C by humans. His 1972 book *The Healing Factor* is considered a classic.

In April 1966 Irwin Stone met Linus Pauling, who found him to be extraordinarily well-informed and convincing. Pauling credits this meeting with Stone as the starting

point of his own interest in vitamin C.

Irwin Stone received many awards and honors during his lifetime, including two honorary doctorates. He was the author of over 120 scientific papers including at least 50 on vitamin C.

Irwin's survivors include his beloved wife of over 50 years, Barbara, and his son Steven, a patent attorney. His memory will be honored and cherished by all of us who were fortunate enough to know him.

Bernard Rimland, Ph.D.

Frederick R. Klenner 1907 - 1984

Fred R. Klenner, M.D., another great pioneer in research on vitamin C, died at the age of 76 on May 20, 1984, just two weeks after the death of his long time friend Irwin Stone. Klenner continued his practice of medicine in Reidsville N.C. until February 1984, seeing as many as 30 to 40 patients a day, until his failing heart caused his retirement.

Klenner's bold and successful use of megadoses of vitamin C during the polio epidemics of the 1940s came to the attention of both Irwin Stone and Adelle Davis, who perceived the enormous value of this approach and were thus stimulated to increase their own efforts to carry the message to the medical profession and the public.

Klenner's use of high-dosage vitamin C in pregnancy resulted in greatly improved health for both mother and infant, and greatly reduced the duration of labor. In addition to his well-known work on vitamin C, Klenner has also published on the use of megadoses of other vitamins; especially the B vitamins in treating neurological diseases.

Klenner has received a number of awards for his important work. His survivors include his wife Ann, their son Fred R. Klenner Jr., M.D., and two daughters.

Bernard Rimland, Ph.D.